

One More Leap into the Dark

THE British government has at last this week decided where to build a third airport for London. The Minister for Trade and Industry, Mr John Davies, seems in the end to have been persuaded by the minority report which Professor Colin Buchanan provided as an appendix to the report of the Roskill commission last December (see *Nature*, 228, 1241; 1970). By doing so, Mr Davies has given heart to all those who have been saying for the best part of a decade that the only civilized places for modern airports must be places where the noise will do comparatively little damage. The difficulty, of course, is that by rejecting the advice of the main Roskill commission, Mr Davies has called in question not merely the competence of the commission, which sat for two years at a cost of more than £1 million, but also the whole method of deciding intricate questions like these. Why have successive refinements of the techniques of cost benefit analysis given such contradictory results? Why has the government now settled for a site in the Thames estuary when the opinions of a whole succession of committees of civil servants have gone the other way? Might it not be better, when choosing the site for a new airport, to blindfold some public dignitary and ask him to stick a pin somewhere in a map?

In case the belief that rationality can help in the solution of important public decisions should be undermined by what has happened, it is important to identify the error in the Roskill commission's argument. After all, nobody can complain that its work has omitted important factors, one of the chief pitfalls in cost benefit analysis. On this occasion, the Roskill commission has sought to quantify most of the variables affecting the decision. There is even, for example, a sophisticated attempt to measure in pounds sterling what is called the "disbenefit" to people living near the alternative sites for the third airport.

During the course of its work, the commission itself produced two quite different analyses—one, towards the end of 1969, seems to have served chiefly as a means of stimulating criticism. The second, on which the final recommendation was based, seems to have been informed by more up to date estimates of the likely rate of traffic as well as of the extent to which traffic in the early eighties will be channelled not through a third London airport but through one of the regional airports instead. In spite of all the sophistication of the argument, however, there seems to be no escape, in arguments like these, from the need eventually to make a decision by comparing very large and necessarily uncertain numbers representing the costs and the benefits at the alternative sites. In circumstances like these, it is often the case that no amount of refinement can make this chancy comparison into a rigorous procedure.

Last December, the Roskill commission's calculation went something like this. At Cublington, the recommended site 50 miles north of London, the cost of building

an airport would at present be £536 million, equivalent to £301 million in 1982 when the sums involved are properly discounted. At Foulness, the site now chosen in the Thames estuary, the corresponding figures are £564 million and £295 million. Initial construction is by far the largest item in the arithmetic of tangible costs—for all the sites considered, the cost of such things as road and rail links (£28.5 million and £38.4 million for road and rail when properly discounted for the Foulness site) is comparable with what must be the error in estimating construction costs. In exactly the same way, the attempts which have been made to estimate the cost to innocent people from the noise generated by the alternative airports, in itself an interesting calculation, give figures such as £22.7 million (discounted to 1982) for Cublington and £10.2 million for Foulness. The difficulty is that the attempt to quantify in money terms a public nuisance such as aircraft noise must necessarily depend on all kinds of untestable assumptions. What Roskill's men did was to guess at the rate at which people would be driven by noise to emigrate from the vicinity of an airport, count up the social cost of such movement and then credit—if that is the word—those who stayed behind with exactly similar costs.

The snag is that this method of estimating the cost of a public nuisance is bound to be enormously in error, and even the Roskill commission acknowledged this with a careful account of what its critics had to say. Different estimates of the cost attributable to noise seem to have differed from each other by a factor of four, with the commission's estimates the lowest. In circumstances like these, would it not be reasonable to suppose that the error in the Roskill calculations must be something of the order of £100 million? This, as it happens, is far greater than the difference between the cost of building an airport at Cublington and at Foulness. To be sure, there is the cost of operating the airport to be considered, as well as that of carrying passengers to and from it, and although it seems beyond dispute that it will cost more to get to Foulness than it would have done to Cublington, the sum of money concerned is not merely a small part of the annual cost of operating the airport but in many ways is comparable with the uncertainty in the present estimate of cost. What this boils down to is the assertion that Foulness would be harder to get to and Cublington would be a greater public nuisance. Obviously there is a limit to the extent to which chalk and cheese like this may be compared with each other. What the Minister for Trade and Industry has done is to weigh the balance in favour of those who would suffer from aircraft noise and against the potential users of the airport. Politically but philosophically as well, this is the right thing to have done.

What is the moral to be drawn from this sorry business? First of all, British governments must recognize that they cannot always count on men with slide rules to



solve awkward problems. Frequently, as with the Roskill commission, there is no escape from what are essentially political problems of striking a balance between one interest and another. But even when it seems proper to attempt cost benefit analysis, it is more important than is usually acknowledged to form not merely numerical estimates of the costs and benefits but numerical estimates of the possible errors as well. Although the Roskill commission has made some efforts in this direction, it has not been as diligent in its attention to sources of error as would have been expected from the expenditure of £1.1 million of public money. The overriding lesson, however, is hardly ever mentioned in the heat of arguments about the rights and wrongs of Cublington or Foulness—the fact that in the work of the Roskill commission, no attempt has been made to regard the alternative airports as parts of an integrated system of air

transport, a network of airlines, air traffic control systems and aircraft designed to move people quickly from one place to another. In the years ahead, however, it may easily turn out to be the case that the best arrangements for long distance air travel will involve a mixture of aircraft types, some for crossing oceans and some for short-haul journeys between major terminals and cities in their hinterland. It is a great misfortune that the airport to be built in the Thames estuary will be put there without due consideration for the full subtlety of the problem. Mr John Davies, the minister, was right to tell the House of Commons this week that there is very little prospect that short or vertical take off aircraft will be developed for passenger traffic before the new airport in the Thames comes into service in the eighties, but that is no reason why the shadow cast on present plans by new concepts in aircraft design should be entirely ignored.

Data Processers of the World Unite

THE proposal of the joint committee of UNESCO and ICSU on what is called a World Science Information System (see page 544) is, on the face of things, harmless and even potentially valuable. Nobody will dispute the starting point for the committee's argument—the assertion that there has in the past few years been such a qualitative change in the character of scientific work that new ways of regarding information are necessary. It is also beyond dispute that one of the most urgent needs is for a greater commitment by working scientists to the development of useful packages of information as well as more efficient systems for regulating cooperation in this field. People should write reviews more willingly, give more thought to the usefulness of the original articles which they send for publication and sneer less when librarians meet to talk about information retrieval. In a world in which mere virtue is no longer a self-sufficient goal, it is only proper that the scientific community should appreciate the harm it inflicts upon itself by allowing the process of exchanging information to be as muddy and as badly organized as it has become. That is what the puritans say, and they are right.

This stern principle is unfortunately only part of the recipe for good management, and those not directly caught up in the grand schemes being hatched in the name of Unisist will be downcast to see how, once again, a preoccupation with the management of information leads to proposals for setting up new committees and new executive offices for servicing them. In this case, when it seems clear that UNESCO as such is making a determined bid for the right to operate an international system of information retrieval, it is also relevant that so far UNESCO's reputation is that of a talker, not a doer. The scientific community is likely for a long time to be suspicious of UNESCO's plans. To be sure, everything will depend not merely on the stature of the scientific committee that will eventually be responsible for advising UNESCO but also on the degree to which the committee can control the organization. Here again, the past is not entirely encouraging. There is bound also to be some scepticism about the plan to deal with the information

relevant to all fields of scientific work within a single framework. The Unisist committee is right to say that one field has often much to learn from others which are in scientific content quite distinct, yet there remains the possibility that comprehensive information services might most easily be developed by concentrating what effort there is to spare on a comparatively narrow front. One important set of doubts about UNESCO's new proposals is that the lessons to be learned from these and similar adventures should be fully digested before more ambitious schemes are mounted. UNESCO may have learned a more efficient way of dealing with these problems, but it is important that it should be closely watched in the years ahead.

There are also doubts about the validity of the notion that information is for practical purposes a commodity to be made up in different kinds of packages to suit different purposes, much as if it were toothpaste being marketed in differently coloured tubes. Like many other documents dealing with what is called the processing of information, the Unisist report is so preoccupied with the tools of the data processers' trade that it has almost entirely overlooked both the quality of information and the purposes which packaging of information is meant to serve. The truth, however, is that information by itself is of hardly any value. Although it is possible to make a living or at least a reputation by collecting and hoarding information in science, the creative function of the content of all the data banks is somehow to change the way in which practising scientists interpret the natural world or seek to exploit it. Two articles in the journals may have identical things to say, but one may turn out to be much more valuable than the other simply because, by being more effectively presented, it is more persuasive. Unhappily, again in the best traditions of librarianship, the Unisist committee has very little to say on points like these, even though the libraries of the world must be full of information which, by being unpalatable, lies undigested or even often unread. The committee's neglect of this central question will only confirm the doubters in their deep suspicion of what is now intended.

Problems of Scarcity and Pollution

IN the first flush of enthusiasm for measures to control the pollution of the environment two years ago, the then British government asked the previously defunct Central Advisory Water Committee to make a study of the ways in which water resources should be conserved and, sometimes, magnified. The result, a report on the subject published last week (HMSO, £0.70), is an interesting illustration of how the management of water resources in Britain, including the control of pollution, turns out to be not so much technical as administrative and legal. To be sure, this discovery is not an immense surprise, for it has been clear from the start that the best assurance that the environment will be free from gross pollution is to have regulations which prevent the feckless from playing havoc with their surroundings. In all the excitement in the United States about the banishment of water pollution as well as in the ringing declarations on the subject such as that by President Nixon a year ago, it seems usually to be convenient to overlook the way in which the dirty rivers of America are a consequence not of industrial activity but of the failure of state legislatures to impose sensible control on municipalities and the failure of the federal government to insist that states should have sensible legislation for this purpose. In Britain, by what seems to be pure luck, the management of water resources and the control of water treatment suffer not so much from too little regulation as from too much. What the committee has discovered is what everybody knew before it began its work—that responsibility is unreasonably divided among organizations with conflicting or at least orthogonal interests.

But where is the balance to be struck between central and local government? The committee is entirely right to say that this is the crucial issue to be decided. Under the scheme which the committee would like the government to devise, something like a dozen regional water authorities would be responsible for the whole forward planning of water resources in Britain. They would, for example, assume the present function of the river boards in licensing the exploitation of natural water. They would also, under the new regime, be responsible for coordinating the plans of local authorities for new sewage treatment plants. The chances are that they would frequently wish to impose some wider plan on the intentions of individual local authorities, and they would have logic on their side.

So does technology have no part to play? One of the most striking passages in the report is that which demonstrates that the annual expenditure on new sewers and sewage treatment plant exceeds £150 million a year, and that the pace of growth of this expenditure has increased steadily for a decade. The committee has understandably been concerned with the anomalies in the present arrangements for administering water resources, but it might well have asked the question whether the present arrangements are as economical as they should be. Is it economic sense that small treatment plants should spring up on the outskirts of every township? Has the linear programming to discover where best to site treatment plants in an integrated network been begun? Is it not high time that the case for an integrated system of water resources

should be based not merely on the qualitative common sense of the water committee's report but also on a calculation, yet to be attempted, of how much money could be saved by proper planning?

In Britain, the most glaring anomaly is that a scarcity of usable water can coexist with a climate so wet and damp that tourists are frightened off. The annual drought in Manchester has almost ceased to make the front pages of the newspapers. Another question neglected by the water committee is that of whether the time has not come for Britain to abandon the notion that water should be supplied to those who use it at a price which is, for practical purposes, independent of the quantity consumed. In all but a few parts of the country, domestic consumers pay an annual charge calculated from the size of their house and not their consumption of water. These are the pricing policies of plenty. This, for example, is how charges should be made for telecommunications now that the cost of providing them has fallen and when many earlier limitations of the capacity which the system could provide have been eroded. With water, the trend is towards scarcity, not plenty. The proper response of water authorities is to ask that people pay for what they use.

100 Years Ago



Pangeneses

I do not much complain of having been sent on a false quest by ambiguous language, for I know how conscientious Mr. Darwin is in all he writes, how difficult it is to put thoughts into accurate speech, and, again, how words have conveyed false impressions on the simplest matters from the earliest times. Nay, even in that idyllic scene which Mr. Darwin has sketched of the first invention of language, awkward blunders must of necessity have often occurred. I refer to the passage in which he supposes some unusually wise, ape-like animal to have first thought of imitating the growl of a beast of prey so as to indicate to his fellow monkeys the nature of expected danger. For my part, I feel as if I had just been assisting at such a scene. As if, having heard my trusted leader utter a cry, not particularly well articulated, but to my ears more like that of a hyena than any other animal, and seeing none of my companions stir a step, I had, like a loyal member of the flock, dashed down a path of which I had happily caught sight, into the plain below, followed by the approving nods and kindly grunts of my wise and most-respected chief. And I now feel, after returning from my hard expedition, full of information that the suspected danger was a mistake, for there was no sign of a hyena anywhere in the neighbourhood. I am given to understand for the first time that my leader's cry had no reference to a hyena down in the plain, but to a leopard somewhere up in the trees; his throat had been a little out of order—that was all. Well, my labour has not been in vain; it is something to have established the fact that there are no hyenas in the plain, and I think I see my way to a good position for a look out for leopards among the branches of the trees. In the meantime, *Vive Pangeneses*.

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OLD WORLD

SOUTH AFRICA

Rate for the Age

by a South African Correspondent

THE Joint Council of Scientific Societies in 1969 undertook a survey on the distribution, qualifications and income of scientists in South Africa. The survey was done by Dr A. P. Burger, director of the National Research Institute for Mathematical Sciences, Council for Scientific and Industrial Research, and his results have now been published (*J.C.S.S. Survey of Scientists, 1969*, obtainable from the Secretariat, P.O. Box 61019, Marshalltown, Transvaal). Since the start of the survey, salaries in all occupations including science have been substantially increased. The maximum salary for university professors, for example, has been increased from R7,200 to R9,900 (£=R1.71). Virtually all salaries have been adjusted to roughly the same extent, however, so that while the data obtained in the survey are probably outdated, the findings are still largely valid.

Predictably, scientists in the public sector were more poorly paid than those in the private sector, while both groups earned considerably less than self-employed members of professions operating for their own gain. As shown also by Masson (*S. Afr. J. Sci.*, **65**, 329; 1969), biologists, possibly owing to their negligible market value in the private sector, were more poorly paid than their colleagues in the mathematical and physical sciences, even though the biologists included a larger proportion of highly trained scientists. School teachers were conspicuously worse off than other groups, even in the public sector. In addition there were fewer teachers between 30 and 45 years of age than above 45 years, suggesting that the poor salary conditions in teaching have been responsible for a regrettably low influx into this profession and/or early loss of young teachers to other professions.

Fortunately, the salary improvements in the past two years have been perhaps more favourable for teachers than for other employees of the public sector, so that the present picture is more encouraging.

A few big employers in the public sector employed 51 per cent of government and semi-government scientists. These employers paid distinctly poorer salaries than the smaller employers in this sector. Government corporations, on the other hand, paid very well, their salaries corresponding to those in the private sector. While higher qualifications, on the whole, led to better salaries, graduates with honours degrees were not noticeably better paid than those with bachelor's degrees.

Recently, concern in the public sector has been mainly for the more junior salary levels and the fact that too few young scientists were being recruited because of the unattractive immediate financial future facing them. The survey shows, however, that concern for salaries of senior scientists is justified. It appears that not only did scientists in the private sector earn considerably more (scientists earning R8,000 per year in government service could expect R14,000 in the private sector), but salaries levelled off more rapidly in the public sector than the private; in the latter, the average scientist at 57 earned roughly R3,000 more than his colleague of 37, while in the former the salary difference was only R800. In the teaching profession the difference was even smaller, only R160 per year. The spread of incomes within each age group was much smaller in the public than in the private sector, and with it "the opportunity to distinguish between staff of superior and lesser merit".

SCIENTIFIC INFORMATION

UNESCO and ICSU Unisist

THE joint committee set up in 1967 by UNESCO and the International Council

of Scientific Institutions (ICSU) to study the problems of scientific information has now reported. The committee, the moving spirit in which has been Professor Harrison Brown, foreign secretary of the United States National Academy of Sciences, is known formally as the Central Committee on the Feasibility of a World Science Information System, translated by the acronym Unisist. The report which has been prepared will be the raw material for an intergovernmental conference in October this year at which UNESCO hopes that there will be established a world science information system.

The synopsis which accompanies the full report says that the need to set up an integrated information system has been occasioned by a qualitative change in the character of science in the past twenty years. One practical result, the report says, is that newly emergent interdisciplinary fields have created the need for the repackaging of scientific information in new forms, often ephemeral. The result is that information services can no longer be left in the hands of scientists, librarians and other specialists. The Unisist committee has come out strongly for a national organization in every country with responsibility for the processing and

MOLECULAR BIOLOGY

MRC Funds Still Flow

IN spite of reports last week that research at the Medical Research Council Laboratory of Molecular Biology in Cambridge is in jeopardy, there seems to be no immediate danger that it will be cut back. Although there are to be economies on expenditure for consumables, no research will be dropped nor will the start of any new programme be delayed.

The reduction in funds for the research councils which was announced last September has meant that the rate of increase of income for the councils will be less than had been planned. The budget of the Medical Research Council as a whole has increased steadily during the past five years. The allocation for the current financial year is £23 million, an increase of 17 per cent compared with that of £19.7 million last year. The overall cut is being passed on to the research units, although newly established units have usually been treated a little more generously than simple proportion would dictate. The MRC Laboratory of Molecular Biology continues to receive more than three per cent of the MRC budget—3.43 per cent this year, compared with 3.17 per cent last year.

These allocations do not, however, take account of inflation, which has eroded most of the increases. In terms of spending power, most MRC units will be in much the same position this year as they were last year. There will, however, be a little more flexibility, for it has been agreed that the directors of individual units will be able to decide for themselves how their allocations will be spent. This means, for example, that a decision could be made to leave a post vacant and instead to purchase equipment.

MRC Molecular Biology (supply estimates)

Year	Recurrent	Capital	Total	MRC grant-in-aid	Per cent spent on MRC mol. biol.
1971-1972	0.71	0.07	0.78	23.0	3.43
1970-1971	0.52	0.10	0.62	19.7	3.17
1969-1970	0.38	0.15	0.53	17.1	3.12
1968-1969	0.32	0.22	0.54	15.3	3.57
1967-1968	0.29	0.23	0.52	14.2	3.69

MRC income and grants made to the Laboratory of Molecular Biology (£ million).

packaging of information. The committee is plainly not in awe of the information explosion, as it is sometimes called, and indeed argues that there are several hopeful tendencies in the present organization of scientific work, from the willingness of organizations and even people to collaborate with each other to the emergence of mechanical devices, especially computers, for the handling of information.

What does the Unisist committee hope for? One theme running through the report is the need to economize in the handling of information. Another, not surprisingly, is the need to standardize information services so as to make them compatible with each other. In particular—and this will no doubt be one of the principles to be settled at the conference in October—the Unisist committee asks that associated countries should survey information services of national, regional or international scope and make plans to integrate these into a “world referral network”; evidently the Unisist committee is not yet confident that it could spell out in detail the way in which such a system should be organized.

The committee is, however, clear that there should be an attempt to develop standard codes and formats for the storage of information in machines, an international registry of scientific periodicals, joint efforts to develop indexing languages and an investigation of the potential use of telecommunications in the processing of scientific information. The committee also suggests research programmes in the development of better library services and the organization of centres for the compilation of numerical data.

On the scientific literature, the Unisist committee takes the hopeful view that “the primary scientific journal, which has traditionally played such an important role in the communication of scientific information, will not be displaced in the immediate future”. It goes on to say, however, that there are many defects in the present system—“authors abuse the privilege of authorship; referees may indulge duplication and error. The time is overdue for a tightened discipline”.

The committee also asks that scientific organizations and societies should cooperate internationally in the management of information as well as the training of people and the conduct of research. Scientists, the committee says, will have to reconcile themselves to a more active role not merely in the dissemination of information but in the acquisition of what they need to know themselves. And in the long run, there is such scope for exploiting new techniques in communications that work should begin now to plan the uses to be made of these facilities. The committee

is strong on the need to draw developing countries into the work on which it has set its heart.

The committee makes no bones about the organization that it would like to see grow up. First, it says, the conference in October should set up an international scientific committee to provide advice and an executive office to manage the programme, the latter within UNESCO. To begin with, the committee considers, it would be sufficient if the permanent office had a staff of twelve and a budget of between \$750,000 and \$1 million.

ROYAL INSTITUTION

More Hard Times

THREE Ministers of Science and Technology in succession have refused government aid to the Royal Institution and unless the director, Professor George Porter, has more success in his applications to Mrs Margaret Thatcher, the venerable building in Albemarle Street may have to close its doors. Indeed, the miracle is, perhaps, that the doors have remained open for so long without substantial financial help.

The RI is in fact a victim of inflation. Its endowment is no longer handsome but its contents are of great value. The statement of accounts published in the most recent annual report shows clearly that in terms of day to day running expenses and maintenance costs, the institution is in serious trouble. The excess of expenditure over income for the year was £9,017 although this was £3,000 less than in the previous year.

When learned societies generally are at a loss to know how to make ends meet, should the Royal Institution's plea for public support meet with especial sympathy? There are several grounds for supposing that it should. In the first place, the institution provides a wide range of activities and opportunities for participation in science, all without financial burden to the public. There are programmes of scientific films, the famous discourses and the invaluable collections of resources material freely available to students of the history and philosophy of science. Every day 500 schoolchildren hear a lecture on an aspect of science, free of charge and without cost to the government or to local education authorities.

Second, there is the fabric and heritage of the institution. The Davy Faraday laboratory is the oldest working laboratory in the country, and was turning out data some seventy years before the Cavendish or Clarendon laboratories were established. Professor Porter claims that “no square footage of laboratory space in the world has turned out so much research of quality”. Restored and renovated, the laboratory will soon be on display to the public.

Apart from money from the BBC for the screening rights of the Christmas lectures and other special science series, the greater part of the institution's income is made up of membership fees and rents. The membership fee is already 7 guineas a year and the institution is plainly reluctant to increase this further, especially as a drive is in progress to recruit new members.

One area in which the institution compares unfavourably with other richer societies is publications. The institution does, of course, publish its *Proceedings* three times a year but this is hardly a money spinner in the class of, say, the *Journal of the Chemical Society*. The *Discourses* are at present in course of publication, but even at the projected price of around £135 a set, these are not likely to repair the institution's fallen fortunes. There is, it seems, a good case for inaugurating a new publication to serve both as a public service and as a source of revenue, but so far no positive steps have been taken in this direction.

There are other, more esoteric solutions—there have been suggestions of a merger between the institution and the British Association, but as the BA would contribute to the union a dowry not merely meagre but mortgaged, the institution may be unwilling to pursue this. Nevertheless, such a merger would make for a degree of rationalization in British popular science.

Whatever the solution, the Royal Institution cannot maintain its present scale of wholly commendable activities without financial aid. The sum involved is only £10,000 or so annually.

CAPS AWARDS

Three Cornered CAPS

THE Science Research Council's scheme for making cooperative awards between industry and universities is holding its own. Its ultimate success must depend, however, on how the aims of the scheme are interpreted by the industrial companies and academic institutions which cooperate. Where there is good agreement between university and industry on what can be achieved, how best to bring about its accomplishment, and how much each party can expect to get out of the relationship, a CAPS studentship can be a rewarding experience. On the other hand, where the relationship between boilersuit and gown is anything less than cordial, the results may be much less happy.

The CAPS scheme began in 1966–67 as a way of chivvying reluctant scientists out of their ivory towers and into industry. It has not been an overnight success—in 1967, some 90 studentships were awarded, and this year the number has risen to just over 200. The principle behind the scheme is the hope

that collaboration in research projects should mutually benefit both industry and university, and that students who might otherwise discard the idea of a future in industrial research can get some idea of what it is really like and, with luck, opt for that sort of career.

According to the SRC, the selection of students for CAPS awards is rigorous although the first essential is not so much academic interest as a viable research project with a sound industrial application. The idea for the project can come either from industry or from a university department, but the project must first be assessed by an independent committee. An individual award costs the SRC about £3,000 over three years. Cooperating industrial companies enjoy such benefits as there may be in a research student's research. Awards are made in mathematics, chemistry, physics and biology. Engineering is for the time being excluded, apparently because it seemed obvious that research for a higher degree in engineering would almost by definition be relevant to industry; now, however, there are signs that this may be untrue, and CAPS awards in engineering might pay rich dividends.

The sponsors hope that CAPS awards will stimulate links between the industrial companies and university departments. The company is expected to provide advice and perhaps equipment for the project and, in return, to obtain such results of industrial value as there may be. Moreover, the student is expected to spend at least three months of his three-year stint working actively with the company. The scheme is, in effect, rather like a sandwich course inside-out—in the CAPS scheme, the meat is on the outside.

How is the scheme working out in practice? On the whole the awards seem to appeal to companies such as ICI and Kodak as well as to the heads of university departments. The question of patent rights was at first a potential difficulty, and the SRC's first attempt to work out an equitable three-way settlement failed. The solution has been for the SRC to renounce all claims to patent rights but to prepare a model agreement for the other two partners and to appoint the National Research and Development Corporation as an arbitrator.

The first batch of CAPS students has now gone through the mill but has shown no conspicuous eagerness to work in industry. This may be something of a disappointment, although it is probably far too soon for lasting judgments to be made.

The cosmic ray detection unit at Durham illustrates how CAPS awards can be most productive. The department has been associated with IRD Limited for many years and three

CAPS students are currently involved on the development of spark chamber particle detectors which are manufactured by IRD and sold to the SRC Nuclear Physics Laboratory at Daresbury—one way of taking in one's own washing. Other CAPS students have not fared as well, chiefly, it would seem, due to poor understanding between the firm and the university department. In one case, the university was looking for financial support from its partner while the industrial company expected that its fundamental research would be undertaken by the university for nothing.

ZOOLOGICAL SOCIETY

National Zoo?

THE promise of substantial government support may mean an end of the hand to mouth existence which has dogged the Zoological Society of London for the past few years. Government grants totalling £1½ million were made last June, and cast a cheerful glow on the society's annual report, published this week.

It has long been the claim of the society that, unlike comparable institutions such as the British Museum or Kew Gardens, it has maintained its public amenities, the zoos at Regent's Park and Whipsnade, without recourse to the taxpayer's money. This seems to have been not so much a piece of justifiable self-congratulation as a reminder to the government that it is the only institution in the world to maintain a national zoological collection supported only by its own resources and whatever private donations it can attract. In 1969, however, after nearly 150 years of relative independence, the society finally appealed directly to the government for support. The immediate response was a short-term loan of £375,000 pending the report of a firm of management consultants on the society's finances.

Unlike those who have pointed out that the controllers of 36 acres of central London (not to mention 500 acres of Whipsnade parkland) have little excuse for losing money, the consultants found that the society was operating as economically as the scope of its activities allowed, and that it would have been regrettable if activities were in any way curtailed. Among the more important of these activities are the society's scientific and educational programmes, on which an annual total of £300,000 is spent. Over 60 per cent of this goes directly to research, a figure matched by no other zoo in the world.

The consultants gave due credit to the society for its progress in implementing its long-term redevelopment plan during the past few years. Since

the inception of the plan in 1958, the council of the society has succeeded in raising more than £3½ million, only £350,000 of which came from government or local government sources. All of this money has been used to regenerate the scientific work and to replace the out-dated and unfashionable enclosures and buildings, many of which have been a feature of Regent's Park for more than 100 years. Today more than half the plan has been completed, and three-quarters of the animals rehoused.

Several years ago, however, the momentum of the redevelopment programme began to decline. The plans for the new primate house, designed in 1966, had to be revised in 1968 to take account of the rise in building costs, and it was only through the generosity of Michael Sobell, who donated £250,000, that it was possible to begin building in 1969. The lion house, built in 1875, was next on the list, but there was no money left in the kitty. The society then appealed to the government for help.

Following the consultants' recommendations, the government made an immediate grant of £650,000 and a further £700,000 over five years. It also decided to waive repayment of the 1969 loan. The first payment has enabled the society to pay off its short-term loans. Under the pressure of the redevelopment programme these were costing nearly £70,000 in interest each year. Savings were, therefore, considerable last year, but they were almost completely cancelled out by increased wages and salaries. The five year grant will enable capital expenditure to continue. Plans for the new lion house can now be drawn up and the near-derelict gardens can be improved. A start will now be made on the long-term plan, prepared in 1969, to landscape Whipsnade Park into a series of "habitat exhibits". Throughout the financial difficulties Whipsnade has, of necessity, been denied its improvements.

Although the latest grant will not enable the society to see its plans through to their conclusion, it does afford breathing space in which to look for more donations and to institute ways of increasing the revenue. One of the major projects set aside for the future is the landscaping of the unattractive south boundary of Regent's Park zoo. The society holds the option on a further 10 acres of the park in this area, and plans to use it to blend the zoo more into the park surroundings. As important to the society as all these material benefits, however, is the mark of confidence implicit in the government's action. It is happy at last that it has been recognized as a provider of social amenities and a generator of scientific achievement worthy of the country's support.

NEW WORLD

Premature Puff for Smoking Beagles

by our Washington Correspondent

AN important study of the relationship between smoking and lung cancer has fallen foul of an insidious hazard awaiting those with newsworthy research to relate, the receipt of too much publicity before publication in the scientific literature. The study, designed to demonstrate the effects of cigarettes on smoking beagles, was presented in February 1970 to a meeting of the American Cancer Society in New York. It has since become the bone of contention in a public dogfight between the American Cancer Society and the Tobacco Institute, the manuscript has been rejected by the *New England Journal of Medicine* and withdrawn from the *Journal of the American Medical Association*, and the paper has only now appeared in *Archives of Environmental Health* after a career that cannot but hinder its judgment before the bench of the scientific community.

The chief authors of the study are E. Cuyler Hammond, vice-president for epidemiology and statistics of the American Cancer Society, and Oscar Auerbach, senior medical investigator at the Veterans Administration Hospital, East Orange, New Jersey. In essence, the study describes the microscopic changes, judged to be indicative of cancer, which were found in the lungs of beagles that had for 30 months been smoking cigarettes through an aperture in their throat. In the ordinary course of events, the paper would have appeared in the scientific literature and its merits or demerits then discussed with reference to material that was fully available. Departure from this scheme of things began with a press conference arranged by the American Cancer Society on February 5 last year after the presentation of the paper to a scientific meeting. The press conference was the opening round in a Tweedle Dum/Tweedle Dee type battle which enhanced the dignity of neither participant. The Tobacco Institute, of course, exists to promote a product that kills thousands of people for the gain of the tobacco industry, but that consideration aside, it deserves at least a sneaking sympathy with the grounds on which it took issue with the American Cancer Society, the fact that the experiments in question remained unpublished and therefore unassailable for many months after the February 5 press conference.

Not content with having Hammond and Auerbach present their results at the press conference, the American

Cancer Society drummed home the message by explaining in a press release that the study was the first time that cigarettes had been shown experimentally to cause lung cancer in a significantly large animal and that the results "should have a significant impact on the smoking of cigarettes in this country, and will probably lead to a reassessment of advertising claims and policies of the cigarette industry". Three weeks later, on February 27, the Tobacco Institute replied with a letter from its executive committee chairman, Joseph F. Cullman, to the chairman of the board of the American Cancer Society, William B. Lewis, making the predictably unacceptable request that the unpublished data of the Hammond-Auerbach study be submitted to a panel of "independent" scientists nominated by the Tobacco Institute. Lewis replied saying that the beagle study "meets the highest traditions and protocol of scientific investigation" and that in any case the report would be "published in the very near future". A second letter from Cullman to Lewis repeated the request for a review panel, this time with the threat—duly implemented—that "if the Cancer Society does not accede to my request, we plan to use every means at our disposal to see to it that the medical and lay public are made aware of our respective positions in this matter".

This letter produced a haughty reply from the Cancer Society. "We do not intend to ask that these two eminent men submit their findings to any selected committee chosen by the Tobacco Institute, or any other group," and Lewis countered the request for review with an equally absurd *ad rem* proposal of his own, that the Tobacco Institute should repeat the Hammond-Auerbach experiments itself if it wished to test their validity. Lewis also added the testimonial that the beagle study was "the result of three and a half years of diligent and brilliant work by two eminently qualified scientists whose findings have been validated by distinguished pathologists of world-wide reputation". The pointless correspondence ended on April 29 last year with a letter from Cullman to Lewis declaring, with some justice, that the American Cancer Society "cannot be the sole custodian and interpreter of the work" and giving warning that the Tobacco Institute would launch a public counter-attack, which the next day it did.

The chief thrust of the Tobacco Institute's campaign was the argument that the results of experimental work as released to the mass media are often oversimplified and lead to conclusions which are not substantiated by the reports of the same work in scientific journals. "This is particularly true," the institute's hand-outs declared, "when, as in the present case, preliminary experimental results are released to the lay press before review by competent editorial boards or other scientific authorities." Continued delay in getting the paper published played into the Tobacco Institute's hands, with the result that by October 12, despite the most authoritative testimonials the Cancer Society could provide, the Tobacco Institute was brazen enough to declare that the beagle study "may be one of the great scientific hoaxes of our time".

Testimonials from the American Cancer Society, however, are not infallible, and in fact it turned out that the manuscript of the beagle study was not so impeccable as to satisfy every referee. The manuscript was rejected for quite different reasons, however, by the *New England Journal of Medicine*, to which it was first sent. In the opinion of the editor, Franz J. Ingelfinger, an article about the paper that had appeared in *Medical World News* contained so much of its substance, including three original micrographs, as to constitute prepublication and disqualify its claims for space in a journal that aims to publish original material. Ingelfinger returned the paper on these grounds alone without sending it out to referees.

The authors' next step was to submit the manuscript to the *Journal of the American Medical Association*, but by now, through no fault of its own, the paper had generated so much feuding that the editor of the journal, Hugh H. Hussey, took the unusual step of sending it out to as many as 18 referees. Because the paper was so controversial, Hussey explained last week, he sought the opinions of a variety of specialists including veterinary and human pathologists and statisticians. Few papers are so perfect as to escape criticism from all of 18 referees, but in fact the suggestions for revision returned by the journal's referees were what Hussey describes as "quite fundamental". The paper, he says, was not worthy of publication in the form in which it was received, a verdict with which it is hard

to reconcile the confident testimonials of the American Cancer Society.

The manuscript was returned to the authors with the referees' comments, but instead of resubmitting a revised paper to the *Journal of the American Medical Society*, Hammond and Auerbach sent the paper to *Archives of Environmental Health*, a prestigious journal but one with a smaller circulation and less cachet than the previous two to which the paper had been offered. Auerbach, who is a member of the advisory board of the *Archives*, said that the editor of the *Archives* had wanted to publish the paper from the beginning and that rather than go once more through the procedure at the *Journal of the American Medical Association*, he and his co-authors had decided to start afresh with the *Archives*.

All the referees' comments were in fact taken into account before submitting the paper to the *Archives*, Auerbach explained last week, but these resulted only in minor revisions. "We changed nothing scientifically. Ever since the day the paper was presented I have never changed one thought on any of the material." Referring to Hussey's description of the referees' suggestions for revision as "quite fundamental", Auerbach says, "We changed the format, the writing, the pictures—if he calls that fundamental, then these were fundamental changes." Asked why the revised manuscript was not resubmitted to the *Journal of the American Medical Association*, and whether he anticipated another delay despite the revisions, Auerbach said, "I have to leave that as it is."

Appearance of the paper in the *Archives of Environmental Health* (21, 740; 1970) has at last made the study available for scientific discussion, but the battle in public still drags on.

Last month the unusual medium of the *Congressional Record* was the vehicle for a savage assault both on the methodology of the beagle paper and on the manner of its treatment by the American Cancer Society. The author of the assault, Victor B. Buhler, of the St Joseph Hospital, Kansas City, and a past president of the College of American Pathology, claimed that "quite remarkable changes" both in wording and in substance had been made between the text issued at the press conference of February 5, 1970, and the version of the paper appearing in the December issue of the *Archives*.

These changes, Buhler says, were responsible for a misleading account of the experiment quoted in the recent report on smoking of the Royal College of Physicians of London, which relied on the version issued at the press conference. "There is obviously a grave risk that the public, and even the

medical profession, may be misinformed and misled by [relying on pre-publication results]. Science can well do without the hanky-panky that results from such unwarranted publicity," Buhler concluded in a letter to Representative Tim Lee Carter of Kentucky. Asked last week in what particular respect the Royal College of Physicians had been misled, Buhler said it would be necessary to compare the report with the press release. He does not intend writing to the *Archives* in order to repeat the scientific criticisms published in the *Congressional Record* because he believes the paper "speaks for itself".

The moral of the story seems to be that publication should, where possible, precede excessive publicity. Delay in publication gave the Tobacco Institute a heaven-sent opportunity to try and discredit what may well be a significant contribution to the cigarette-cancer issue. The authors of the paper were either unlucky or unwise in allowing the substance of their paper to appear in *Medical World News*, but for which the paper might have appeared without fuss in the first journal of choice. But in the editor of the *New England Journal of Medicine* the authors faced a stern opponent of manuscripts which have been published in part elsewhere. "We have a policy that if material has been extensively published in medical news media such as *Medical World News*, then we consider it already published just as much as if it had appeared in the established medical literature," Ingelfinger says. (Ingelfinger's views on prepublication have been laid out in a recent article in *Science* (169, 831; 1970) in which he specifies that his journal's attitude "would be influenced in a negative way if the principal ideas of an article, as well as its crucial data and most important figures, had already appeared in a medical news medium—just as the effect would be negative if the identical items had been published by a paradigm of the staid medical literature".)

Unlike some extremists on this issue, Ingelfinger has no objection to brief accounts appearing in the general or medical news media of papers read to scientific meetings. Difficulties begin when the public relations people of various societies start pressurizing authors to give press conferences so as to publicize the meeting. "If the American Cancer Society had not engaged in such extensive publicity, the ultimate course of events would have been much more favourable for all concerned," Ingelfinger said last week. Auerbach is one who would probably agree with this verdict—"I would never present a paper to the press in the same way again," he says. "I would give the press just a thumbnail sketch, with no

pictures or charts, and I would consult first with the editor of the journal in which I expected to publish the paper."

PHYSICS

Chicago Tries Harder

from a Correspondent

NEARLY 30 years have passed since the late Enrico Fermi directed the achievement of the first self-sustaining nuclear chain reaction on the University of Chicago campus. That historic accomplishment took place in wartime secrecy with an assemblage of such on-campus colleagues as Glenn Seaborg, Arthur Compton, Walter Zinn, Norman Hilberry, Samuel K. Allison, Herbert Anderson and Leo Szilard. For a time after the Second World War, the nuclear physics group at the University of Chicago enjoyed an international reputation. Several of the graduate students in physics went on to win Nobel prizes, among them Chen Ning Yang, Tsung Dao Lee and Owen Chamberlain. In the 1950s, as the anchor men on the faculty moved to other universities while the university vainly sought to rehabilitate its ghetto-ringed neighbourhood, major centres of physics research became stronger at other prominent institutions of higher learning—Berkeley, Harvard, Columbia, Michigan, Wisconsin and Cornell.

Now, as construction of the \$250 million National Accelerator Laboratory nears completion some 40 miles north-west of the Chicago campus, the university is again allocating money, time and energy to revitalize its physics department. This is being done under the direction of John Wilson, the vice-president and dean of faculties who formerly served as a deputy director of the National Science Foundation, and Robert G. Sachs, a physicist-administrator who directs the university's Enrico Fermi Institute of Nuclear Studies.

The new emphasis at Chicago is on high energy physics. The university recently announced the addition to its faculty of James W. Cronin, a senior member of the team of Princeton University physicists who, in 1964, conducted the experiment at the Brookhaven National Laboratory in New York which upset the formerly fundamental concept of time reversal invariance. While on leave from Princeton University, Cronin has been working with the laboratory's experimental facilities group. At the University of Chicago he will join a growing group of physicists which hopes to develop closer ties with NAL. Among his colleagues at Chicago will be Valentine L. Telegdi, an experimentalist who was a member of one of three teams to have experimentally

proved the nonconservation of parity theory for which two former Chicago students (Chen Ning Yang and Tsung Dao Lee) won the Nobel prize; Yoichiro Nambu, a pioneer in the studies related to the regularities in the relationships between strange particles and one of the first to suggest the existence of the omega vector meson; Roger H. Hildebrand, who with a colleague discovered the ratio of intensities of two cosmic ray components to provide an important clue to the understanding of the origin of cosmic rays; and John A. Simpson, widely known for his experimental and theoretical studies in high energy astrophysics.

In a related development, Chicago recently appointed Albert V. Crewe as the dean of its Division of Physical Sciences. Crewe is no newcomer to "big science"; from 1961 to 1967 he was director of the Argonne Laboratory, 25 miles west of the university's campus. There, as head of a \$300 million dollar research complex, he directed the work of more than 1,000 scientists and 3,000 supporting staff members and helped to build the zero gradient synchrotron. Returning to the Chicago campus, Crewe designed and built a scanning electron microscope and devised a technique that revealed single atoms in molecular structure for the first time.

Geographically, the University of Chicago is in an advantageous position to develop close rapport with the new laboratory. Robert R. Wilson, the laboratory's director, also is listed on the university's physics faculty; he too is on leave from Cornell University. Despite its developing strength in high energy physics, however, there are students of elementary particle physics who feel that the University of Chicago still must add a few more "stars" to its faculty if it is to achieve pre-eminence again in physics.

Buying in top grade physicists may be less expensive than signing on football stars, but it takes rather longer for the new blood to make an impact on the team's reputation. Chicago's reputation as a physics institution, as measured by the quality of its graduate teaching faculty, has declined from fifth place in the table of US universities in 1957, to tenth place in 1964, according to surveys prepared by the American Council on Education. The council's most recent report, based on questionnaires distributed in 1969, lists Chicago's physics faculty as equal ninth in the top league, tying with Cornell and being beaten by Berkeley, CalTech, Harvard, Princeton, MIT, Stanford, Columbia and Illinois. The downward slide seems to have been halted, but will even the attraction of the nearby National Accelerator Laboratory help restore the vanished glories of Fermi's day?

NATIONAL ACADEMICS

Merit and Power

by our Washington Correspondent

IF there existed an organization such as a national academy of successful business and government executives, its membership would probably not differ greatly from that of the National Academy of Engineering. The new intake into the academy consists of the following personages (the names are not important):

The Deputy Secretary of Defense, an Assistant Secretary of the Navy, the Deputy Director of the Office of Science and Technology, the Vice-President of Bell Laboratories, the Manager, Milwaukee Operations, of the General Motors Corporation, the Vice-President for Research and Development of Beckman Instruments Inc., the Chief of the Hydraulic Design Branch of the Office of the Chief Engineers of the Department of the Army, the Assistant Vice-President for Engineering of the American Telephone and Telegraph Company, a Vice-President of the Ford Motor Company, the Executive Vice-President of the Esso Research and Engineering Company, an Assistant Director of the Atomic Energy Authority, the Chairman and Chief Executive Officer of the Aluminium Company of America, the Honorary Chairman of Texas Instruments (who doubles up as Mayor of Dallas), the Chairman of the Board and Chief Executive Officer of General Dynamics, the Assistant Commissioner for Science and Technology of the Environmental Protection Agency, a General Manager of the Westinghouse Electric Corporation, a Lieutenant General who is commander of the Space and Missile Systems Organization of the US Air Force, the President of the Raytheon Company, another executive from Bell Laboratories, another executive from the Raytheon Company, and a Vice-President from the Lockheed Aircraft Corporation. In addition the Chief of the Illinois State Geological Survey and seven academics, all of the rank of professor, dean or chairman, have made the grade.

The fact that each of these 29 new members holds some important office as well as being doubtless an engineer of merit suggests that merit alone is not a sufficient qualification for entry into the academy. Indeed, most of new entrants are credited in the academy's announcement of their election not with any specific engineering accomplishment but with extraordinarily diffuse achievements which imply skills in business management rather than engineering, for example, "leadership and direction

of the Minuteman weapon system", "personal leadership in the development of ballistic missile technology", "contributions to aerospace management", "accomplishments in managing the development and applications of new technologies".

The National Academy of Engineering is allowed to select members on a somewhat wider basis than does the National Academy of Sciences of which it is a recent offshoot. Members may be chosen on the basis either of important contributions to the literature of engineering, or for "demonstration of unusual accomplishments in the pioneering of new and developing fields of technology". Whereas individual merit in science is usually easy to recognize, it could be that engineers, who tend to work in large teams, may not be able to demonstrate their individual merit except by rising to the top of the management tree. Even so, it is hard to understand how the National Academy of Engineering, with so many thousands of American engineers to choose from, can exhibit so little imagination as to draw its new membership almost exclusively from the top brass of the Defense Department, Ford, General Motors, General Dynamics, Lockheed and so forth.

A selection that is so obviously dependent on factors other than merit is bound to be injurious to an institution whose prestige and purpose depend on its being an elite. The academy's sister organization, the National Academy of Sciences, is facing critical and often hostile scrutiny as it plays the increasingly difficult role of tendering and being seen to tender independent advice to the government, but the necessary appearance of independence is not exactly assisted by the stratum from which the National Academy of Engineering likes to draw its members. Nor does it show any exquisite sensitivity to the objections of potential critics for the Academy of Engineering to appoint as chairman and vice-chairman respectively of its membership committee Dr Edward E. David, the President's science adviser, and Dr Alexander H. Flax, president of the Institute for Defense Analyses. It goes without saying that Dr David is not a man who would allow his political sympathies to interfere in any way with his job as chairman of the NAE membership committee, but is the academy really unable to find a more neutral figure to undertake this chore?

A self-perpetuating elite is an institution rather like a monarchy; both are useful as long as they preserve their dignity, but since in concept they verge so close to the ludicrous, a single false step can be fatal. With its new membership list the National Academy of Engineering seems to have lost its sense of the absurd.

Short Notes

Reactor in Limbo

TRIGA mark II, a small nuclear reactor being constructed for Columbia University, may never go critical. In the wake of protests from local residents, the Atomic Safety and Licensing Board of the AEC refused permission for the reactor to begin operation on the grounds that too little was known about potential hazards to the surrounding populace. The decision, which is the first time a licence has been refused for any reactor in the United States, will be of interest to the operators of the 72 other research reactors now in use, including 22 Trigas. Columbia's reactor, on which \$671,000 of AEC and NSF money has been lavished over the past 11 years, is completely finished apart from its fuel unit.

Up, Up and Away

NASA has announced the names of the 108 US and foreign scientists chosen to advise on the Grand Tour missions to the outer planets. Altogether some 500 scientists submitted proposals to the agency last October. The successful Grand Tourists are grouped into 13 teams, each with a team leader, whose task is to determine the best spacecraft configuration and combination of experiments for the missions. A recent report by the Space Science Board of the National Academy of Sciences said that NASA could not afford to include Grand Tour missions in its present budget without distorting the overall science programme. NASA has ignored this advice but Congress, now considering NASA's budget for 1972, may not.

Environmental Manpower

LAST year the manpower engaged in protecting the environment amounted to some 35,000 engineers and 37,000 scientists. According to estimates made by the Environmental Protection Agency, the actual demand was for 44,000 engineers and 72,000 scientists (*Environmental Science and Technology*, April 1971, p. 314). To make significant improvements in environmental quality 70,000 engineers and 95,000 scientists will be needed by 1975, rising to 105,000 and 75,000 respectively by 1980. These projections are based on the less than absolute certainty that the present and ensuing Administrations intend to put serious money into rehabilitating the environment.

Professors Get Poorer

ACADEMIC salaries last year failed to keep pace with the cost of living, the American Association of University Professors reports. The average salary of faculty members from lecturer to professor was \$13,233, an increase of

only 5.0 per cent, while the consumer price index jumped 6.0 per cent. This is the first time since 1949 that the average increase in salary levels has been less than the rise in the cost of living. When fringe benefits are included, however, the total compensation of the academic community rose last year by 6.2 per cent. Average salaries in 1970 were \$18,300 for a professor, \$13,800 for an associate professor, \$11,300 for an assistant professor, \$9,000 for an instructor and \$11,100 for a lecturer. "1970 was a bad year for the academic profession," the AAUP report concludes. "Whether it ushers in a disastrous decade remains to be seen."

Muskie Opposes Pipeline

THE Alaska pipeline project has gained yet another opponent in the person of Senator Edmund S. Muskie. Last week Muskie wrote to President Nixon urging that the permit for the pipeline be denied because of the hazards it presents to the environment. "Fortunately, it appears that a trans-Canada route may present greatly reduced risks," Muskie told Nixon. The senator's opposition to the Alaskan pipeline is based on two critiques of the environmental impact statement prepared by the Department of the Interior to assess the effects of the proposed pipeline. One critique, by F. Stuart Chapin of Alaska University's Institute of Arctic Biology, stresses the indirect damage the project would cause to marine life because of tanker traffic to the port of Valdez. Cleaning of ballast tanks will amount to the release of 12 barrels of oil a day into the Valdez arm, with incalculable effect on marine organisms. Robert R. Curry, professor of environmental geology at the University of Montana, describes as "dangerously inadequate" the seismicity data cited by the Department of the Interior in assessing the risk of earthquakes to the pipeline.

Privacy Study by NSF

THE citizen's right to privacy and its abuse by government agencies, particularly those which handle their data with computers, is currently fashionable. Recent hearings before Senator Sam J. Ervin's committee on constitutional rights revealed that the army had spied on civilian politicians such as Senator Adlai Stevenson III, and had encoded dossiers on some 8 million people at Fort Holabird, Maryland. The National Science Foundation has now entered the scene with a \$160,000 grant to Arthur R. Miller, a Michigan University law professor whose book *Assault on Privacy* was one of the starting points of the Senate hearings. Miller's project is to study how information is handled by social scientists and government social welfare agencies in the United States and abroad.

Prizemen Reapprized

UNTO him that hath shall it be given is a precept closely followed in the handing out of academic prizes. For example, five of the seven scientists receiving prizes from the National Academy of Sciences this week have already received prizes before. For two of them, Subrahmanyan Chandrasekhar and James D. Watson, the academy awards represent their sixth scientific trophy.

Chandrasekhar has already notched up the Bruce Medal of the Astronomical Society of the Pacific, the gold medal of the Royal Astronomical Society, the Rumford medal of the American Academy of Arts and Sciences, the National Medal of Science for the United States and the Royal Medal of the Royal Society. To these spoils he now adds the Henry Draper medal and \$1,000 in cash.

Watson, besides having a share in a Nobel prize, is the recipient of the John Collins Warren prize of the Massachusetts General Hospital, the Albert Lasker award of the American Public Health Association, a Research Corporation prize and the Eli Lilly award. This week the National Academy is awarding him the John H. Carty medal and a cheque for \$3,000.

Why do committees with prizes in their gift prefer to honour those already laden with prizes, rather than seek to encourage a young and relatively unknown scientist (as is often the stated intention of the bequest setting up the prize)? Could it be that by some strange inversion of roles the awarding of a prize to distinguished recipient honours the giver rather than the taker? Viewed in this light the distribution of scientific prizes is as much a self-indulgence for the prize committee as an over-indulgence of the prizeman. Perhaps bequeathers of prizes could rest rather more assured of the honest execution of their intentions if they were to stipulate that their eponymous awards be bestowed only upon virgin prize-men. But would there then be more prizes around than scientists worthy of notice by the prize-givers?

NEWS AND VIEWS

Tracking Electrons in the Magnetosphere

THE discovery of the Van Allen belts of magnetically trapped particles surrounding the Earth was the precursor of a rapid increase in the use of satellites and rockets to probe both the radiation in the vicinity of the Earth and the Earth's magnetic field. During the past decade more and more experiments have been designed to examine in detail the properties of the Earth's magnetosphere—that region around the Earth in which the magnetic field is reasonably ordered and at least approximately characteristic of the field of a magnetic dipole, though distorted by the solar wind of plasma.

Such phenomena as auroras, for example, have been known for hundreds of years but it has only been the magnetospheric work of the past few years which has provided the real clue to their mechanism. It is now established with almost complete certainty that they are caused by electrons of energy a few keV impinging on the atmosphere and exciting atoms and molecules. Some of the techniques used for studying artificially generated auroras have not been as elegant as others, however; the Starfish nuclear detonation at a height of 400 km in 1962 was an example of a particularly uncontrolled and controversial experiment in which large numbers of electrons were released. But more finely controlled experiments have also been successfully used. In 1969, for example, pulses of electrons were fired from a rocket in such a way that they spiralled along the magnetic field lines and into the atmosphere. The photographic recording of the auroras generated by these electrons gave probably the first data on the sizes and locations of auroras created by electron beams of known intensity and energy.

Having succeeded in producing artificial auroras almost at will and measuring their properties from the ground, the next logical step was to look at the exact behaviour of electron beams of well defined energy and intensity as they follow their spiral paths and mirror near the magnetic poles. On page 564 of this issue of *Nature*, Hendrickson *et al.* describe their recent rocket experiment which was quite similar in principle to that carried out in 1969. Instead of injecting beams of electrons at such a height that most of them contribute to auroras in the upper atmosphere, the conditions of the flight were arranged so that a large proportion of the electrons were reflected magnetically back to the rocket where they could be detected and their energies and intensities measured.

Not surprisingly the height to which the Aerobee rocket had to be flown from the launching site at Wallops Island, Virginia, was rather higher than in 1969—about 350 km compared with 270 km. The exacting requirement that a beam of electrons a few tens of metres across should be intercepted by the rocket after reflexion made rocket control a critical feature of the experiment. The fact that the helical paths do not follow a simple north-south route but are deflected in an easterly direction because of the gradients in the Earth's magnetic field only serves to increase the problem.

The potential difficulties of experiments of this type are highlighted by the very small amount of time for which meaningful measurements can be made. Although

the rocket flight lasted about ten minutes and the electron gun was firing for a substantial fraction of this time, the rocket was only moving on the correct magnetic shell and at the correct eastward velocity for about one minute. (The magnetic shells are imaginary surfaces along which electrons of given characteristics are constrained to spiral.) The spinning and precession of the rocket create another less serious problem but some electrons are inevitably injected towards the mirror point at the north and some to the southern point.

Surprisingly, some of the most useful data came from reflexion measurements made when the southward and upward motion of the rocket was such that the rocket was moving to a higher or lower magnetic shell during the bounce period (that is, between the time of injection of a particular pulse and the detection of its reflexion). It so happens that, because the magnetic dipole which approximates the Earth's magnetic field does not coincide with the Earth's centre, the altitudes at which genuine magnetic mirroring would take place for electrons from the rocket in the southern hemisphere are quite small. There is therefore a high probability that scattering by atoms, molecules and ions causes the electrons to undergo a mirroring process at a greater height than expected for true magnetic mirroring. It is clear that because the pitch angle of the helical path becomes smaller as the mirror point is reached the electrons spend a high proportion of their time near this point and the precise position at which the electrons are sent back the way they came has a marked effect on the bounce period. Hendrickson *et al.* have found that their observed bounce period is in quite close agreement with the predicted figure assuming that scattering plays an important part in the mirroring process. Another consequence of the scattering effect is that the beam will not be as well collimated after reflexion and some of the electrons will diffuse over a finite spread of magnetic shells. This explains why electron echoes could still be detected at the rocket even when it was not moving on the same magnetic shell for the whole of the bounce period. The effect of scattering and the nature of the transition region at which magnetic reflexion ceases to play a dominant part in changing the direction of an electron are, of course, important for the development of auroral theories and the data reported will be useful as a comparison with some theoretical Monte Carlo simulations.

A further parameter of the magnetosphere, the electric field, could also be important in the formation of auroras but direct field measurements at high altitudes are almost non-existent. The conclusions about the size of this field which Hendrickson *et al.* are able to make are very general and rather inexact, but this is inevitable. A radial electric field at the equator, for example, would modify the easterly drift of the electrons, and if it had been sufficiently large the rocket would never have been in the correct position to intercept the reflected bunches. The fact that echoes were actually detected leads Hendrickson *et al.* to place an upper limit of $700 \mu\text{V m}^{-1}$ on this electric field configuration.

EPIGRAPHY

The First Script?

from our Archaeology Correspondent

RECENT discoveries in Bulgaria suggest that the use of writing, or proto-writing, or at least of signs resembling writing first appeared in prehistoric Europe about 4000 BC. This early date, however, may not be accepted by all archaeologists.

As early as 1903 Balkan scholars suggested that the signs incised on pottery of the Vinča culture of neolithic Serbia might constitute an early form of writing and in 1929 this view was reiterated by Gordon Childe, who compared the signs with those seen in the early Aegean and in predynastic Egypt. Interest seemed, however, to wane a little after that time, although the possibility of direct Aegean influences in the art and religion of prehistoric Serbia has been warmly advocated by Milošević and other Yugoslav prehistorians.

This view was dramatically reinforced by the discovery in Romania of the Tărtăria tablets in what appeared to be a context of the Vinča culture (*Dacia*, 7, 1; 1963). The signs on these three small baked clay plaques were accepted by the distinguished Sumerologist, the late A. Falkenstein (*Germania*, 43, 261; 1965), as representing a script closely resembling the pictographic writing seen on the "protoliterate" tablets from Uruk in Mesopotamia, datable to some time after 3000 BC. The discovery was hailed by some scholars, such as Vladimir Milošević and Sinclair Hood (*Antiquity*, 41, 99; 1967), as documenting direct links between the Balkans and the Aegean in the early third millennium BC, and perhaps contacts with Sumer as well.

The find is made yet more interesting, and much more puzzling, when radiocarbon dates for the Vinča culture are taken into account, especially if these dates are calibrated by means of the Californian tree ring sequence as proposed by Suess (in *Radioactive Dating and Methods of Low Level Counting*, 143, IAEA, Vienna, 1967); this would put the Vinča culture two millennia earlier, considerably earlier than the first emergence of any script in the Near East or indeed elsewhere.

In the face of the apparent paradox that a script similar to the first of the Near East was in use much earlier, there were two possible arguments allowing an escape from the unwelcome conclusion that the Near East was taught to write by the Balkans. The first was to view this "script" in Yugoslavia and Romania as a purely local development, quite unconnected with anything seen in the Near East, in spite of the view of Falkenstein that the two were

related. The second was to deny the early date of the Tărtăria tablets; this argument was advanced on stratigraphic grounds by E. Neustupny (*Antiquity*, 42, 32; 1968), and Milošević and Hood reach a similar conclusion by denying the validity of the radiocarbon dating method as a whole.

There the matter rested, until the discovery at Karanovo in Bulgaria of a baked clay disk or "seal", 6 cm in diameter, bearing a linear design interpreted by the excavators G. I. Georgiev and the late V. Mikov (*Arkheologiya*, 11, 12; 1969) as written signs constituting a script. The inscription was hailed by the distinguished Bulgarian philologist, Professor Vladimir Georgiev, as "une vraie sensation scientifique". And so it is, for its context at Karanovo shows it to be contemporary with the Yugoslav Vinča culture, and in this way it serves to confirm the early date of the Tărtăria tablets. Moreover, radiocarbon dates from Karanovo itself place it before 3300 BC in radiocarbon years, and hence perhaps before 4000 BC in calendar years, long before any known Near Eastern script.

This find cannot easily be shrugged off, followed, as it is, by the report of a similar find of the same period, this time from north-west Bulgaria, where, at the interesting late Neolithic site of Gradeshnitsa, Bogdan Nikolov has found an analogous and slightly earlier

inscription (*Arkheologiya*, 12, (3), 7; 1970). This again has been accepted as writing by Vladimir Georgiev. Can it then be supposed that writing first appeared in the Balkans around 4000 BC, perhaps a millennium before the development of the first ideographic script in the Near East? Or does the find support the arguments of Hood and Milošević that radiocarbon dating, and *a fortiori* its dendrochronological calibration, are a snare and a delusion?

The solution lies perhaps in a closer examination of the meaning attached to the terms script and writing. There is no evidence that the Balkan signs ever developed into the useful system for storing information which is seen in Sumer and early Egypt, nor do the Balkan inscriptions form sequences of signs in which the same sign is seen to recur in different contexts as do ideograms in a true script. Yet there seems no reason to deny that these curious incisions may have held a meaning, a symbolic value, evident to their makers and perhaps to others. In this sense at least they may be regarded as ideograms or pictographs.

One eminent Sumerologist at least has certainly accepted them as writing. If this is admitted and the radiocarbon chronology is followed, it seems difficult to escape the conclusion that these signs constitute the earliest writing in the world.

Activated Charcoal foils Fastidious Smut

To grow an organism successfully in culture still ranks as rather more of an artistic than a strictly scientific accomplishment, and the literature (not to mention the bench space) of its practitioners is littered with the dusty discarded Petri-dishes of past failures. Obligate parasites take pride of place in this catalogue of non-success, and so it is particularly pleasing that in next Wednesday's *Nature New Biology*, P. R. Day and S. L. Anagnostakis of the Connecticut Agricultural Experiment Station report the successful growth *in vitro* of the corn smut (*Ustilago maydis*) dikaryon, for this unpleasantly effective pathogen has so far resisted all attempts at culture.

The trick which ensured success where there has been so many previous failures was the incorporation of one per cent (w/v) activated charcoal in an otherwise minimal media. The addition of the charcoal may facilitate removal of a substance produced by the dikaryon and which is inhibitory to hyphal growth.

The life cycle of *Ustilago*, as with all smuts, is passed in three phases. The diploid resting phase which is characterized by the teliospores is formed in

the tissues of the host. These undergo meiosis on germination to form yeast-like haploid cells. It is the fusion of two of these non-pathogenic haploid cells which gives rise to the pathogenic dikaryotic mycelium, a mycelium in which pairs of compatible nuclei are associated but not fused.

In the charcoal-modified medium of Day and Anagnostakis, the dikaryon formed a slowly growing branched mycelium composed chiefly of empty cells. There were no clamp connexions and the formation of teliospores in culture was not observed, so clearly the charcoal medium does not completely mimic the environment of the host plant.

Apart from the considerable advance in that yet another stubborn organism has been induced to grow in environmentally controlled conditions, what does the work of Day and Anagnostakis mean for plant pathology? The point of most importance is that the pathogen is now open to much more detailed genetical and physiological examination: investigations which would be very complex if they had to be carried out with the smut still on the host plant can now be executed in a simpler manner.

TUMOUR VIROLOGY

European Conviviality

from a Correspondent

AS the old hands insisted from the outset, if there are lapses in the quality of the science presented at meetings of the European Tumour Virus Group they are more than compensated for by the pervading conviviality; and those people fortunate enough to have spent three days last week (April 19–21) at Bad Wimpfen, West Germany—venue of the group's sixth meeting—were given good cause to continue to spread this gospel. The meeting was a considerable success in all respects, the scientific not excepted.

Dr T. Graf (Max-Planck Institute, Tübingen), for instance, reported detecting recombination between two mutant strains of Rous sarcoma virus incapable of transforming secondary chick fibroblasts. One of these mutants, of subgroup A, lacks about 15 per cent of the single stranded RNA genome of its wild type parent. The second mutant, a subgroup D virus carrying a point mutation, has a genome smaller than that of the subgroup A mutant. Chick fibroblasts infected by either mutant alone are not transformed but cells co-infected with both are transformed and yield progeny virus particles, some of which are recombinants. They transform chick cells, belong to subgroup D and have a genome larger than the subgroup D mutant but smaller than the subgroup A viruses.

Of the several reports from Dutch groups working on mouse mammary tumour virus (MMTV), Dr O. Mühlbock's (Netherlands Cancer Institute, Amsterdam) was outstandingly interesting. His group has found striking differences in the response to Bittner virus (C3H.MTV) and GR.MTV between congenic strains of mice which differ by one gene only—they carry different alleles of the H2 histocompatibility gene. Of the mice with the H2b allele 14 per cent develop mammary tumours after being fostered on milk containing Bittner virus compared with an incidence of 89 per cent among congenic mice carrying the H2a, d, f, k or m alleles similarly fostered. By contrast, after fostering on milks containing the GR.MTV, the incidence of mammary tumours among H2b mice is 41 per cent and among H2a, d, f, k or m mice 52 per cent. Clearly the antigenic composition of mice profoundly influences their response to MMTV. And Dr G. de The (International Agency for Research on Cancer, Lyon) commented that a comparable situation may exist in man. Evidence is accumulating which suggests that presence of the W5 allele of the HLA system may perhaps minimize the pathogenicity of

EB virus infections. And Dr A. Vaheri (University of Helsinki) reported experiments done in Hanafusa's laboratory (New York City), which must quicken the pulses of the manufacturers of rifampicin. At concentrations in the range 40 μ g to 100 μ g/ml. this antibiotic significantly inhibits the multiplication and reduces the viability of chick cells transformed by Rous sarcoma virus, whereas similar doses have no detectable effect on parallel cultures of untransformed cells.

Dr B. Hirt (Swiss Institute for Experimental Cancer Research, Lausanne) reported that polyoma virus and SV40 virus particles contain six polypeptides, three of which are also present in empty capsids. Apparently none of these polypeptides yields fingerprints identical to those of host cell histones; they may well therefore all be specified by the viral genome, in which case they would account for about 75 per cent of its total coding capacity. According to Dr J. S. Pagano

and his colleagues (Swiss Institute for Experimental Cancer Research, Lausanne), one of the three polypeptides common to virions as well as empty capsids, and the three polypeptides unique to virions, may have a role in regulating transcription of the viral genome; these proteins certainly reduce the amount of RNA transcribed by *Escherichia coli* transcriptase.

Some adenoviruses, like polyoma virus and SV40, are oncogenic for rodents and Dr J. Williams (Institute of Virology, Glasgow) described some of the properties of the extensive suite of adenovirus 5 temperature sensitive mutants he has isolated during the past year. They fall into nine complementation groups, and at least one mutant at its non-permissive temperature seems to lack the capacity to transform rat embryo cells, and no less than six, at the non-permissive temperature fail to induce interferon but induce it at the permissive temperature. The Glasgow group seems to have struck a rich vein.

Mammalian RNA-DNA Hybridization Improved

SINCE the first RNA-DNA hybridization experiment eleven years ago, the technique has been widely and successfully used in many simple organisms; however, its serious application to mammalian nucleic acids has proved to be a problem of an entirely different order of magnitude. In next Wednesday's *Nature New Biology*, Melli *et al.* describe a new method of analysis with which they have been able to demonstrate for the first time hybridization of RNA which is complementary to the non-reiterated fraction of mammalian DNA.

It is well known that the mammalian genome consists in some sequences which are highly reiterated, and others which are either unique or only repeated a few times. Previous experiments have only demonstrated hybridization of RNA with the reiterated fraction of the DNA, because hybridization with the unique fraction takes place too slowly to be observed by the usual "saturation" technique.

In any hybridization experiment in solution, RNA-DNA hybrid formation is always in competition with DNA renaturation. The membrane filter technique using immobilized DNA was introduced to overcome this problem (Gillespie and Spiegelman, *J. Mol. Biol.*, **12**, 829; 1965), but Melli and Bishop have already found (*Biochem. J.*, **120**, 225; 1970) that this method has a serious drawback in mammalian hybridization, namely that the extent of reaction is dependent on the sheared size of the DNA. They therefore reverted to the solution method, and

effectively got round the problem of the two competing reactions by keeping the DNA in large excess. The theory of the method is based on the kinetic analysis of DNA renaturation devised by Britten and Kohne (*Yearbook Carnegie Instn.*, **65**, 78; 1965); the proportion of DNA renatured is a function of the parameter "Cot" (product of DNA concentration at zero time, and time), and when a segment of DNA is 50 per cent renatured the value of Cot (Cot_{0.5}) is simply the reciprocal of the DNA renaturation rate constant, the latter being a measure of genetic complexity. From this the reiteration frequency of a particular sequence can be obtained, and by keeping the DNA in excess, Melli *et al.* observed the RNA-DNA hybridization as a side reaction superimposed on the predominating DNA renaturation reaction.

When applied to RNA from *Escherichia coli*, the method worked well, but with ribosomal RNA from rat liver, agreement with the theoretical curve was not so good, suggesting that this method of hybridization is not free from inherent difficulties.

The importance of Melli *et al.*'s work, however, is the demonstration that rat RNA synthesized *in vitro* and heterogeneous nuclear RNA will hybridize with the non-reiterated fraction of rat DNA. This is something of a milestone in hybridization history, but it is a sobering comment on the complexity of mammalian nucleic acids that it has taken more than a decade of hybridization experiments for this formal demonstration to be achieved.

GENETICS

Neurone Mapping

WITH the current emphasis on experiments involving interference of one sort or another with the organism under study, Dr Sidney Brenner's talk to the Royal Society on April 22 was a startling reminder of what can still be achieved by means of pure description. Or almost pure, for his work involves the creation of nematode mutants by dosing with methyl ethane sulphonate, as well as genetic mapping of the ensuing mutations. Nonetheless, the most impressive part of Dr Brenner's recent work from the practical point of view is his painstaking neurone-by-neurone description of the nematode nervous system.

His aim essentially is to take the "molecular" out of molecular genetics and use its powerful methods for studying the specification of systems of cells in whole organisms. Nematodes were selected for several reasons. First, they are unquestionably animals, which, said Dr Brenner, could not strictly be said for amoebae and still less for slime moulds. Second, they have a 3½-day life cycle and each nematode produces 300 larvae at a time. Third, they can be stored in a state of suspended animation in liquid nitrogen until needed—in other words, as Dr Brenner said, you can keep a file of mutants. And fourth, they have a singularly convenient reproductive arrangement. They are in general hermaphrodite, so that there is no difficulty in producing a completely isogenic population from one nematode if one is wanted; but about one nematode in 2,000 is male so that crosses are also possible. Male nematodes can be distinguished by their behaviour ("the same way that I know I'm male").

Because he wished to look at the nervous system, Dr Brenner was primarily interested in mutations which could be seen to interfere with movement. From his studies of mutants, he now has a genetic map of which an interesting aspect is that although there are extensive empty spaces on the chromosome diagram, the sites on which mutations were found seem to be saturated; Dr Brenner does not believe that this is an artefact of the mutagen he used. If this is true, it should be very interesting to evolutionary theorists.

Nematodes are about the diameter of an erythrocyte, so electrophysiology is out of the question. Dr Brenner has instead built up a three-dimensional map of the nematode nervous system using serial electron microscopical sections; he described some of his findings from three wild type specimens and three ("... well, as the result of an accident, 2.9") mutants which he has designated UNC30. It turns out

that the organization of the wild type nervous system is invariant; and more interesting still, that some of the neurones which displaced in the mutants are displaced in an invariant fashion. To find out precisely how these structural aberrations relate to the behaviour of the organism, Dr Brenner will need a total three-dimensional map of the nervous system of each phenotype. He is now engaged in trying to find out how to program a computer to store such a map at the same time as the genetic map, in the hope of elucidating the logic of the genetic control mechanism. This kind of approach—that of looking for the logic of a system rather than its detailed chemistry—is undoubtedly one that is gaining ground.

GEOLOGY

African Events

from a Correspondent

IN spite of the broad theme "Frontiers of Geological Research in Africa", the sixth colloquium on African geology held from April 14–17 at the University of Leicester dwelt for the most part on two topics: the detailed structure of the Precambrian basement and the mega-tectonics and magma control of the African plate. A notable feature of the colloquium was its informality: no speeches except a few impromptu ones, no delegates, no

official business and no publications. The organizers merely made sure the purpose of the meeting was fulfilled—that geologists swapped ideas about Africa.

Mineralization, like granulites, received less attention than it should have done. Dr R. W. Henley (University of Manchester) suggested an ingenious thermal convective system whereby gold is precipitated in solid rock by a mass transfer of auriferous solutions across thermal gradients.

Much more was said when it came to discussing the structure of the African basement. Dr R. Caby (University of Montpellier) gave a clear exposition of the Precambrian history of the Hoggar Massif in the Sahara, and showed that the Suggarian and Pharusian both belong to one major orogenic cycle deformed 2,000 million years ago, and again later in the Pan African event ~600 million years ago, but Dr G. Vitel (University of Algiers) thought this was an oversimplification and redefined a more limited, early Suggarian facies of deformation. Dr P. W. G. Tanner (University of Leeds) gave an excellent account of Ruwenzori. Ancient gneisses >2,500 million years old are overlain by Toro metasediments deformed ~2,000 million years ago, and all have been affected by the Pan African event of 600 million years ago. Professor V. V. Belousov (Moscow State University) said that although Ruwenzori is well known to

Isoacceptor tRNA as an Enzyme Inhibitor

AMONG the mysteries of protein synthesis is the problem of isoacceptor tRNAs. It is unclear why several tRNA species which accept the same amino acid are universally encountered or why the pattern of these isoacceptor species sometimes changes when changes in cell metabolism occur such as during differentiation or viral infection. The work of Jacobson (reported in next Wednesday's *Nature New Biology*) provides an important clue to one possible physiological function of such a multiplicity of redundant tRNA species. He finds that one of the tyrosine tRNA isoacceptor species from *Drosophila melanogaster* can inhibit the enzyme tryptophan pyrrolase present in a vermilion mutant, although it does not affect the same enzyme from wild type *Drosophila*.

He takes as his starting point the earlier finding that tryptophan pyrrolase activity is practically absent in this vermilion mutant, although normally present in wild strains of *Drosophila*. But, by the simple expedient of treating crude homogenates of the mutant flies with T_1 ribonuclease, to destroy all the RNA therein, he was able to regenerate

tryptophan pyrrolase activity within these extracts. On attempting to discover more exactly how this is brought about, he found that total unfractionated tRNA from wild type flies can inhibit once again the activated tryptophan pyrrolase. When this tRNA is fractionated chromatographically, it becomes clear that one of the tyrosine isoacceptor species is in fact responsible for the observed inhibition. He reports briefly the result of a remarkably elegant experiment confirming this finding. If the vermilion mutation is suppressed by the introduction of a further mutation, tryptophan pyrrolase activity is partially restored and the chromatographic peak attributable to the inhibitory tyrosine tRNA isoaccepting species disappears.

If these findings are more widely applicable, in that other iso-accepting tRNAs are also involved directly in regulating the activities of enzymes participating in intermediary metabolism and biosynthetic or degradative pathways, this would clearly be a major addition to the rule book of cell regulation as it is at present constituted.

students as a horst it is in fact not a horst but is an arch-like uplift with a few minor faults around it. Dr J. R. Vail (University of Khartoum) recorded that Sudan still provides many enigmas in the interpretation of basement structures, but that the Mozambique Belt can be traced from south to north, if perhaps in rather a zigzag fashion.

On the topic of mega-tectonics in Africa, flexibility of the African plate apparently gives the key to a new extra mechanism of global tectonics. Dr H. Faure (Laboratoire de Géologie Dynamique, Bellevue, Paris) described undulations of the plate with wavelengths of the order of 100-1,000 km, amplitudes (uplift) 10^3 - 10^4 m, over periods of 10-100 million years, each distinguished by individual histories of erosion and sedimentation. Professor B. C. King (Bedford College, London), on whom was conferred on April 21 the Murchison Medal for his work in Africa, forcefully demonstrated the marked difference between oceanic and continental rift systems. Dr M. J. Le Bas (University of Leicester) took the differences further and showed (see *Nature*, **230**, 85; 1971) that many areas such as Kenya mark igneous provinces of characteristic per-alkaline magma (often including kimberlites) which are upswollen portions ("swells") of the African plate some 1,000 km across. It seems that the whole Earth has from time to time been deformed and rifted by these gigantic swells, caused by the degassing and/or volume expansion of parts of the Earth's interior. Professor R. A. Reyment (University of Uppsala) likewise demonstrated, from a very different angle, that the continental plate behaved in a most flexible manner, and he tilted and warped a plastic scale model of the African plate to simulate Earth movements and to reproduce known Cretaceous regressions and transgressions in West Africa. Professor A. J. Whiteman (University of Ibadan) also domes and rifts Nigeria and relates the rifting to the opening of the Atlantic Ocean.

M. H. Tazieff (Paris), who arrived half way through the colloquium hot from Etna, showed film taken a few days previously on Etna. He also described, again supported by the most magnificent filming, the ocean-rifting character of the northern Afar in Ethiopia, chiefly salt plains plus volcanoes, and pointed out the deplorable lack of geophysical stations in eastern Africa—a view echoed by Professor R. M. Shackleton (University of Leeds) and Dr M. A. Khan (University of Leicester).

Looking to the future, Professor R. M. Shackleton showed that more geophysical work should be undertaken, whether it be to discover more mineral deposits or to predict earthquakes and

volcanicity or merely to understand better the processes of nature in Africa. Perhaps some results will be seen at the next colloquium to be held in 1973.

NUCLEIC ACIDS

Isolating Messengers

from our Cell Biology Correspondent

DETERMINING the sequence of an RNA molecule has become these days—thanks chiefly to the work of Sanger and his colleagues—so much a matter of routine that the chief problem is finding RNAs worth the effort of sequencing. Enough of the small RNAs of *Escherichia coli* and other organisms—the transfer RNAs, 5S

RNAs and the enigmatic bacterial 6S RNA—have been sequenced to make the prospect of more of the same downright dull; the elucidation of sequence of *E. coli* ribosomal RNA is well on the way to completion and numerous groups are tackling one or other of the RNA phage RNAs. These molecules are of course the only messengers which can to date be obtained pure and in large quantities and it should not be long before the complete sequence of R17, for example, can be announced. Obviously the sequencers would love to get their hands on other messengers, particularly those of eukaryotic cells; that would restore excitement to their work and that is also why Blobel's work (*Proc. US Nat. Acad. Sci.*, **68**,

Changing Shape of Deception Island



THE 1970 volcanic eruption on Deception Island in the Antarctic which partly destroyed a small island formed by a previous eruption and scattered ash and volcanic bombs over a substantial area, may have been a comparatively minor foretaste of what is to come. This is the conclusion of two geologists at the University of Leeds who, under the auspices of the Instituto Antártico Argentino, took part in an international survey of the changes to the island after the eruption on August 13. Their report, which is published in next Monday's *Nature Physical Science*, includes this photograph of some of the new volcanic centres.

Deception Is. is basically horseshoe shaped and encloses a large flooded caldera known as Port Foster. The earliest recorded eruption there seems to have taken place in 1842, but apart from the probability of two further eruptions in 1910 and 1920 and some fumarolic activity the island seems to have been dormant until December 1967 when there began a series of events of which last year's eruption is the latest.

The 1967 eruption led to the forma-

tion of a new island, the "1967 island" in Telefon Bay on the north-west side of Port Foster and there was an associated eruption farther to the east. Two years later there was a fissure eruption on the eastern side of the island and then last year there was more intense activity from an arcuate series of craters stretching from the south side of Cross Hill in the north-west of the island across Telefon Bay to the foot of Goddard Hill to the north-east. Among other things this activity led to the formation of a new strip of land across Telefon Bay, it partly destroyed the 1967 island and it enlarged the crater in the south-west of this former island. This crater now forms the largest of three interconnecting water filled craters, shown here, between the northern foot of Cross Hill and the remnant of the 1967 island.

All the eruptions in the past three years occurred on the inner side of the caldera and Baker and McReath believe them to be connected with movements and instability associated with the caldera fault. They say that further adjustments may take place anywhere in the caldera fault zone.

832; 1971) may attract a large audience.

In the past, attempts to isolate eukaryotic messengers have involved exposing polysome preparations to either detergents or chelating agents. The former procedure releases all the RNA species in polysomes and leaves the problem of separating the messenger RNA from the transfer, 5S and ribosomal RNAs. The latter procedure results in the release only of the messenger and some transfer RNA but the messenger is found complexed with protein. To avoid these problems Blobel has developed a recipe for treating polysomes with puromycin at high ionic strengths, the net result of which is the dissociation of the ribosomes and the release of naked messenger and transfer RNAs which are readily separated. Using this procedure Blobel obtains from rabbit reticulocyte polysomes an RNA which sediments at 11.3 S whereas the other procedure for isolating globin messenger from these polysomes yields a 9S RNA. A simple calculation suggests that this 11.3 S RNA may have about 230 bases in addition to the 450-odd bases needed to code for globin. It would be no surprise if these additional bases formed sequences at the 5' and/or 3' ends of the globin messenger which are not involved in coding, for that is what the partial sequences of the RNA phage RNAs lead us to expect. And how widely applicable is this puromycin procedure? Although Blobel has worked chiefly with polysomes he says that it may be generally useful.

The basis of Blobel's procedure is, of course, the reaction between peptidyl-tRNA and puromycin—an analogue of aminoacyl-tRNA—to yield free peptidyl-puromycin. Raacke (*Biochem. Biophys. Res. Comm.*, **43**, 168; 1971) has constructed space filling models of puromycin and peptidyladenylic acid (to represent the terminus of peptidyl-tRNA) to investigate the stereochemistry of this reaction. In short he finds puromycin can assume a U-shaped configuration and "hug" the terminal adenine residue of the peptidyl-tRNA such that the amino-group of the antibiotic is favourably placed to react with the carbonyl group of the peptidyl-tRNA. All this apparently takes place at the peptidyl site of the ribosome to which the adenine of the peptidyl-tRNA is bound. Raacke envisages that the dimethyladenine of puromycin interposes itself between this adenine and its binding site. The puromycin is then bound to the peptidyl site and the peptidyl-tRNA is bound to the antibiotic by hydrophobic attraction of stacked bases, the dimethyladenine and methoxybenzene of the antibiotic alternating with the terminal adenine and penultimate cytosine of the peptidyl-tRNA.

CANCER

Aggressive Lymphocytes

from a Correspondent

THE notion that there exists a "natural" defence mechanism against the growth of malignant cells is deep rooted in the folklore of cancer research. The evidence in the distant past has been scanty, but reinforced by the will of those investigators who saw the possibility of manipulation of the immune mechanism as a means of control of cancer. Perhaps the biggest objection has always been that if there is a defence mechanism why does it fail so often and why do so many people die with cancer? To say that many of them smoke too much is irrelevant to the present argument.

The concept of the tumour specific antigen has been adduced largely from work with experimental animals and many studies have exemplified such antigens and attempted, in the main unsuccessfully, their characterization. But a recent article by the Hellströms and their associates (*Intern. J. Cancer*, **7**, 226; 1971) helps both to reconcile some previously conflicting ideas and to indicate the road ahead for those interested in tumour immunology.

The basic data, which derive largely from previous work of the Hellströms,

are that the blood lymphocytes from human patients with a variety of tumours can specifically kill neoplastic cells, *in vitro*, from the same patients. In addition, in many instances cells from tumours of similar morphological types from other patients can also be killed. The failure of the aggressive lymphocytes effectively to reduce the malignant cell population in the host of origin has been attributed to the inhibitory effect of blocking antibodies. It is envisaged that in some way these antibodies, which are produced as part of the complex of immune processes, prevent the lymphocytes from reaching, recognizing or destroying their target cells.

The latest article tests the effect that serum from cancer patients can have in preventing lymphocytes from killing tumour cells *in vitro*. A high proportion of sera were effective and ostensibly specific in that they only blocked the reactions between lymphocytes and tumour cells which derived from patients with a similar tumour: host relationship to the serum donor. Hellström and his colleagues point out that their methods provide an *in vitro* index of the magnitude of both cellular and humoral components of the anti-cancer response in patients and they could eventually provide diagnostic and prognostic tools for the cancer therapist.

Long Term Variations of the Plasmopause

In the next issue of *Nature Physical Science*, J. Oksman of the University of Oulu, Finland, proposes annual and sunspot cycle variations in the position of the terrestrial plasmopause.

In the 1930s it was realized that the magnetic field of the Earth could not simply be that of a dipole, because observations of the low frequency variations in the field intensity (micropulsations) showed the field to be compressed on the daylit side of the globe. In 1931, Chapman and Ferraro (*Terr. Magn. Atmos. Elect.*, **36**, 171; 1931) produced a simple model of this compression produced by the interplanetary flux of charged particles (plasma) flowing out from the solar corona.

The interaction of this flux, the solar wind, with the geomagnetic field has been studied intensively over the past decade. It has been shown that the plasma in the vicinity of the Earth is contained within a magnetospheric boundary defined by the solar wind velocity and particle density. By day the magnetosphere—the region within the boundary—has a dimension of order 10 Earth radii (R_E) but at night the boundary is extended into a long magnetospheric "tail".

In the early 1960s it was believed that

the ionization density within the magnetosphere showed a smooth fall off with increasing distance from the Earth. But in 1963 it was demonstrated, from an extensive analysis of the characteristics of audible frequency natural electromagnetic signals (whistlers), that there was a marked discontinuity or "knee" in plasma density at a distance, from the Earth, of the order $3R_E$ (D. L. Carpenter, *J. Geophys. Res.*, **68**, 1675; 1963). Just within the knee the density is around 100 electrons per cm^3 but outside the density it is only a few electrons per cm^3 . The high density region is now known as the plasmasphere and its boundary is termed the plasmopause.

Oksman proposes that the observed variations in the paths of whistlers and most of the observations of geomagnetic micropulsations in a particular frequency band, can be explained if it is assumed that there are annual and secular (sunspot cycle) changes in the size of the plasmasphere. The annual variation deduced is of order $1R_E$ with a smaller secular variation. The motions, it is suggested, are linked with the changing tilt angle of the geomagnetic axis to the ecliptic plane, and Oksman believes that this factor may also explain ionospheric anomalies.

TAXONOMY

Nematode Morphology

THE scanning electron microscope is revealing all to the taxonomist. Fortunately, it usually seems to confirm or extend previous descriptions of species made by eye or with the optical microscope, so that drastic revisions do not usually have to be made. In the case of the parasitic nematode genus *Syphacia*, the scanning electron microscope has made possible the examination of *en face* features which are important taxonomically, as C. G. Ogden now reports (*Bull. Brit. Mus. Nat. Hist., Zool.*, **20**, 253; 1971). Ogden has found that the head in this genus falls into four distinct patterns which may be useful in delimitating groups of species. For example, in *S. citelli*, *S. pallaryi* and *S. transafricana* the lips are reduced in size and have a cuticular thickening giving them a triangular shape as is shown in this illustration of the *en face* view of the head of *S. citelli*.

OBESITY

How Fat Men Respond

Experimental Psychology Correspondent
A POSSIBLE clue to the root cause of obesity in man has been provided by the apparently bizarre behaviour of rats with experimentally induced damage of the hypothalamus. For many years it has been known that the syndrome associated with lesions of the centromedial hypothalamus has included over-eating up to the stage where the animal has become immensely fat, but with a disinclination to expend any effort for food, and an abnormal finickiness. In a recent issue of *American Psychologist* (**26**, 129; 1971) S. Schachter has drawn an extensive analogy between the widely documented behaviour of these animals and observations of his own and his associates on fat people.

Schachter does not argue that indi-

viduals who have a tendency to become fat have a hypothalamic imbalance, though this may be the case. Rather he points to many instances of parallel between the behaviour of fat rats and fat human beings in an attempt to extract some common principle. The principle he infers is that in both cases obesity is produced, and is accompanied by an over-responsiveness to external stimuli and release from control of the internal stimuli reflecting physiological needs that play a major part in regulating body weight at normal levels.

How this apparent dependence on salient external cues affects human eating habits was first shown in an experiment by Nisbett (*Science*, **159**, 1254; 1968) in which fat and normal men who had not eaten lunch were offered (as part of a more elaborate procedure) a plate of one or three sandwiches, and were told that if they wanted more they should help themselves from the refrigerator which contained plenty. The subjects of normal weight ate the same mean number of sandwiches irrespective of how many were on the plate, and this number (approximately two) was significantly greater than the number eaten by fat men when only one was on the plate, and significantly less than the number eaten by fat men when three were on the plate. In one of Schachter's experiments on a similar

theme, subjects ostensibly taking part in an experiment which involved filling in questionnaires were offered some nuts while doing it. About half the subjects of normal weight took nuts whether they were shelled or not, but whereas nineteen out of twenty fat subjects ate nuts without shells, only one in twenty fat subjects ate nuts if they had shells on them.

Striking though these experiments are, perhaps even more unexpected is that fat persons are also in some sense more responsive to external stimuli in conditions not related to eating. Fat subjects actually performed faster in a task where a response with right or left hand had to be made respectively to the appearance of the left or right light in display. In a proof-reading task fat subjects made significantly fewer errors than normals under quiet conditions, but were significantly less accurate when working under distracting conditions.

Schachter seems to have made a powerful and surprising case for the idea that fat people seem to react more readily than normals to external stimuli—and that this may have benefits as well as drawbacks. If he is right then, paradoxically, fat people should have less trouble than normal ones in sticking to diets. To keep food out of mind their major problem is to keep it out of sight.

Peyer's Patches and the Thymus in Newborn Mice

SOON after the pioneering work of Miller and of Good and their respective colleagues had established that the thymus in some way regulated the development of the other lymphoid organs and of the immune function, a search began for the mechanism. It was an attractive postulate that a hormone was released from the thymus which in some way affected the capacity of lymphocytes external to the thymus to respond to antigenic stimulus, and some evidence for such a view was adduced (J. F. A. P. Miller and D. Osoba, *Nature*, **199**, 653; 1963). But it was also shown that cells could emerge from a thymus grafted into a neonatally thymectomized mouse and, in spite of some initial scepticism of the scale of this process, it is now widely accepted that there exist substantial numbers of thymus-derived cells in the adult mammal.

Raff, in a now classic series of studies, has shown that the frequency of these cells varies from organ to organ but that (for example) some 60–70 per cent of the lymphocytes in the axillary lymph node of a mouse are of thymic origin. In the Peyer's patches, which are closely associated with the gut, a rather lower figure of around 30 per cent was noted. Of considerable

interest in this context is the suggestion of Joel, Hess and Cottier, in next Wednesday's *Nature New Biology*, that in the mouse, within a few days of birth, about 60–75 per cent of the cells present derive from the thymus. These findings are not as might seem at first sight incompatible. Raff's determinations were made on adult mice using the presence of cells with the θ antigen as an indicator of thymic origin whereas Joel and his associates labelled cells inside the thymus with tritiated thymidine and picked them up later in the Peyer's patches by autoradiographic scanning. There is little reason to doubt the validity of both methods, and Joel *et al.* conclude, probably correctly, that their high values relate to a situation in which antigenic stimulation from the intestinal flora is just setting in. The corollary is that once the responses are established relatively fewer thymus-derived cells are involved.

These new findings are of interest in another context in that it has been suggested that the gut-associated lymphoid tissue in the mammal acts as an equivalent to the bursa of Fabricius which in birds is regarded, like the thymus, as a primary lymphoid organ (K. E. Fichtelius, *Exp. Cell Res.*, **46**, 231; 1967).

RIBOSOMES

Picking up the Pieces

from our Molecular Biology Correspondent

In many a laboratory, especially since the impact of Nomura's work on step-wise reassembly has made itself felt, ribosomes have been scoured with salts, tanned with aldehydes and devoured with nucleases in attempts to extract from them fragments of RNA still associated with proteins. By some way the most encouraging and informative study so far is that of Allet and Spahr, which has just appeared in the *European Journal of Biochemistry* (19, 200; 1971). This is a polished piece of work, which gives rise to some thought provoking conclusions: treatment of 50S subunits of *Escherichia coli* with pancreatic ribonuclease under mild conditions introducing a single break in the RNA chain. This becomes apparent when the RNA is extracted: gel electrophoresis shows the progressive conversion of the 23S chain into two fragments, which differ in their oligonucleotide maps, and only one of which contains the 3' terminal sequence. The break in fact occurs two-fifths of the way along the chain from the 5' end.

The two fragments evidently remain cemented together by proteins, but when the salt-labile "split proteins" are dissociated by treatment with lithium chloride, they separate and can be collected from a sucrose gradient. When the components of the two pieces were separately analysed, a startling discovery came to light: only two proteins were unique to each fragment. These, one would be tempted to infer from Nomura's results on the 30S subunit, may be the primary binding species, which associate with the RNA and direct the uptake of further proteins, and the correct folding of the particle. The remaining fifteen or so "core" proteins are distributed in varying but reproducible proportions, between the two fragments. To define the specificity of the interaction more explicitly, Allet and Spahr then examined the binding of labelled "split proteins" with the separated core particles. Both core particles are able to bind significant amounts of the various split proteins, though some of these show a preference for one or the other. When the core particles are mixed, however, there is a large increase in the extent of binding of many of the split proteins, and the 50S subunit is in effect regenerated. Such cooperativity of protein uptake was of course described by Nomura and his colleagues in the assembly of the 30S subunits from the vestigial particle, containing only a few primary structural proteins. On reflexion therefore the results of Allet and Spahr can be seen to make good sense. The structure of the 50S subunit is evidently maintained

by a network of binding sites on the proteins, and when the RNA is cleaved, some species remain anchored at one end, some at the other. The primary binding proteins, which direct the re-assembly, bind non-cooperatively and uniquely to one or other fragment of the RNA.

A more rudimentary ribonucleoprotein particle can be obtained from eukaryotic ribosomes by treatment with EDTA, and contains messenger, rather than ribosomal, RNA. Thus far such particles, and their proteins, have been poorly characterized, an omission which has now been rectified to a noteworthy extent by a study from Chantrenne's laboratory (Lebleu *et al.*, *ibid.*, 264). In the first place, under more stringent conditions of sedimentation a contaminating particle is resolved. This sediments at 8S, compared with 15S for the messenger complex, and contains 5S ribosomal RNA and a protein of 45,000 molecular weight—presumably a ribosomal protein. The 15S complex, freed of its impurity, contains only the messenger, and two proteins of high molecular weight, one of them especially at 130,000 (estimated by detergent-gel electrophoresis) much larger than anything normally characterized as a ribosomal constituent.

The 15S particle associates strongly with 40S subunits, and the isolated messenger also binds to an appreciable extent. If, however, the subunits are first washed with deoxycholate, the messenger fails to interact, whereas the messenger-protein complex binds with undiminished efficiency. Conversely, polysomes washed with deoxycholate before treatment with EDTA release free messenger instead of the 15S particle. The proteins in the 15S particle are evidently "factors", vital in some way for utilization of the messenger.

An interesting paper by Herzog, Ghysen and Bollen (*Mol. Gen. Genet.*, 110, 211; 1971) concerns the "dissociation factor" in *E. coli*, which is thought to be responsible for dissociating the 70S ribosomes into subunits after their traverse of the messenger, in preparation for re-initiation. In a mutant strain of cells, dissociation of monosomes by lowering the magnesium concentration is distinctly inhibited. The ribosomal protein pattern is identical with that of the wild type, and it emerges that it is the dissociation factor, which can be prepared by a salt wash, that is defective, when tested on wild type ribosomes. The effect vanishes when an amber suppressor is present, and is therefore an amber mutation.

Electromagnetic Noise generated in the Ionosphere

IN the forthcoming issue of *Nature Physical Science*, D. G. Cartwright and P. J. Kellogg of the University of Minnesota discuss the results of a new rocket-borne experiment carried out in the ionosphere. They have detected electromagnetic radiation associated with an electron beam, of controlled flux and energy, injected into the magnetosphere from the rocket.

The background to the experiment is described by R. A. Hendrickson, R. W. McEntire and J. R. Winckler, also at Minnesota, in this issue of *Nature* (page 564). In the experiment, more than 3,000 short pulses of electrons, of 35 to 45 keV energy and at such pitch angles that they become trapped by the geomagnetic field, were injected at altitudes above 150 km. These electrons were observed to bounce between the mirror point near the rocket and that at the conjugate point, and back, in 0.62 s. As the electrons also drifted eastwards on a constant *L* shell ($L \sim 2.5$), they were observed by detectors aboard the rocket which was launched eastwards from Wallops Island, Virginia.

The electric field of electromagnetic radiation within the frequency range 16 Hz to 10 MHz, generated by the electron beam, was measured by equipment mounted on the ejected fibreglass nose cone of the rocket. While the electron gun was firing, radiation was

observed at frequencies ~ 5 MHz, between the local plasma frequency and the upper hybrid resonance frequency, and also at frequencies < 1 MHz. Čerenkov emission from the beam of electrons is thought to be responsible for the radiation, which propagates at low phase velocities in the extraordinary and whistler modes respectively. Radiation observed at ~ 2 MHz, less than twice the electron gyro-frequency, is consistent with the first Bernstein mode in a warm plasma; the particle-wave interaction producing this radiation is not understood. A spin modulated band of noise at ~ 8 kHz is interpreted as being noise at the lower hybrid resonance frequency caused by argon ions which were emitted to keep the payload electrically neutral while the electron gun was firing. Čerenkov radiation is again the favoured emission process with propagation taking place in the whistler mode.

The important conclusion of this work is that the electron beam loses less than only 1 millionth of its energy to plasma instabilities or to wave emission. Cartwright and Kellogg do not, however, understand all the phenomena observed; marked changes in the characteristics of the signals are observed part way through the flight at the time of the (rather sinister) "black cloud".

Late Miocene Marine and Non-marine Time Scale in Europe

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Argon isotope dating on the island of Samos contributes to the reconciliation of continental and marine time scales in the Mediterranean basin; the first appearance of *Hipparion*, widely accepted as the criterion for the beginning of the Pliocene in land mammal successions, has been shown to be middle Miocene.

THE appearance of the three toed horse, *Hipparion*, in Neogene faunas of Eurasia is held by most vertebrate palaeontologists to mark the beginning of the Pliocene. The consensus has long been that the *Hipparion* datum is 10 m.y. or older¹. On the other hand, radiometric and other geophysical calibration of the fossil microplankton zonation scheme²⁻⁵ indicates that the base of the Pliocene in the marine definition may be as young as 5 m.y. (ref. 6). This article is an account of the direct dating of one of the best known examples of a Eurasian *Hipparion* fauna, and a discussion of the relationships of radiometrically calibrated marine and non-marine faunal successions in the later Neogene of the Mediterranean and western European regions, where the terms Miocene and Pliocene take their original meaning.

Age of the Samos Faunas

The Neogene strata of the Mitilini district on Samos consist of approximately 750 m of monoclinal volcaniclastic sediments dipping north-east with two major freshwater limestone bodies roughly 50 m thick approximately 200 and 350 m above the lowest exposed part of the sequence. Torrent-bedded marble conglomerates, derived from local basement outcrops, are prominent in the lower beds. The basin was mapped (1967 and 1968), chiefly in order to locate and sample strata suitable for dating. As a preliminary measure, the strata were called units 1-5 in ascending order, with the two major limestone bodies called units 2 and 4.

The greatest part of the large collection of Cainozoic vertebrates from Samos, including most of the specimens collected by Major⁷, Schlosser⁸, and Brown⁹, come from the "Adriano" or quarry 1 site, the same as our sample site 106, in unit 3 calcareous volcanic sandstones and siltstones approximately 30 m below the upper limestone. A smaller collection, from Brown's quarry 5, seems to belong to a level stratigraphically above the upper limestone, about 1 km to the north-west⁹; unfortunately, we could not find this locality, and the beds above the upper limestone were not sampled for dating.

The dated samples were all (except GM-101) taken from pumice-rich layers between the two limestones, GM-106 from a thin, calcified pumice-breccia about 5 m above fossil bone *in situ* in the rear wall in quarry 1, and the others from

massive, chalky-white pumice breccias with a porous, styro-foam-like texture. Thin sections of the analysed specimens all contain uncompressed pumice fragments with scattered phenocrysts of sanidine and very subordinate biotite and trachyte lava fragments. The mineralogy of the pumice fragments is uniquely the same throughout each thin section, and apparently throughout each sample, indicating that each pumice-rich bed had its origin in separate episodes of eruption and transport; such accumulations, although apparently re-sorted in water, cannot have been far distant in time or space from an eruption centre, and are evidently related to eruptions in the Cappadocian pyroclastic province on the nearby Turkish mainland, where ignimbrites and tuffs of similar mineralogy are associated with *Hipparion* faunas¹⁰.

Sanidines were extracted by water elutriation of crushed and sieved pumice breccia, followed by magnetic removal of mica, rock fragments and remaining pumice. X-ray diffraction of the sanidine concentrates showed patterns of high-sanidine¹¹ ranging in composition from approximately Or₃₅ to Or₄₀ for the first five samples, and Or₅₀ for GM-106. No other mineral phases were detected. Duplicate splits from each concentrate, weighing about 0.2 g each, were irradiated with fast neutrons in the core of the research reactor at Aldermaston to generate ³⁹Ar from ³⁹K, and then analysed on the 'Omegatron' mass-spectrometer for atmospheric, radiogenic and neutron-induced argon isotopes¹². A single heat-step at 200° C was used to drive off adsorbed atmospheric argon and argon from any low-temperature mineral phases present before the samples were fused. The results (Table 1) are calculated to the 95% confidence level. (The variation between the replicated splits seems to be related to their position in the sample holder during irradiation; this being so, the lost replicate of GM-102 would have been given an older age than the surviving sample, and its average age would have been a few tenths of m.y. greater.)

GM-106 and GM-105 come from levels near the top of unit 3, and GM-102, GM-103 and GM-104 are from a richly pumiceous section from 2 m to approximately 30 m above

Table 1 Argon Isotope Analysis of Irradiated Sanidine Samples

Sample	$J \times 10^{-2}$	% ⁴⁰ Ar Atmo- spheric	R	Age (m.y.)
GM-106, Or ₅₀	3.84	77.2	0.1236	8.9 ± 0.9
	3.63	50.9	0.1164	8.0 ± 0.8
GM-105, Or ₄₀	3.95	45.4	0.1296	9.6 ± 0.8
	3.79	38.4	0.1266	9.0 ± 0.7
GM-104, Or ₄₀	3.92	44.3	0.1214	9.0 ± 0.7
	3.77	51.5	0.1286	9.1 ± 0.8
GM-103, Or ₃₅	3.77	48.2	0.1035	7.4 ± 0.6
	3.92	43.1	0.1132	8.4 ± 0.7
GM-102, Or ₄₀	3.79	51.9	0.1287	9.2 ± 0.7
GM-101, Or ₃₇	3.63	45.1	0.271	18.5 ± 1.5
	3.84	35.0	0.289	20.8 ± 1.7

J is a factor derived from isotope analysis of control samples paired with the test samples, which gives the neutron flux gradient in the sample holder. R is the ratio of radiogenic ⁴⁰Ar to irradiation-produced ³⁹Ar in the sample. The second sample of GM-102 was spilled in transit.

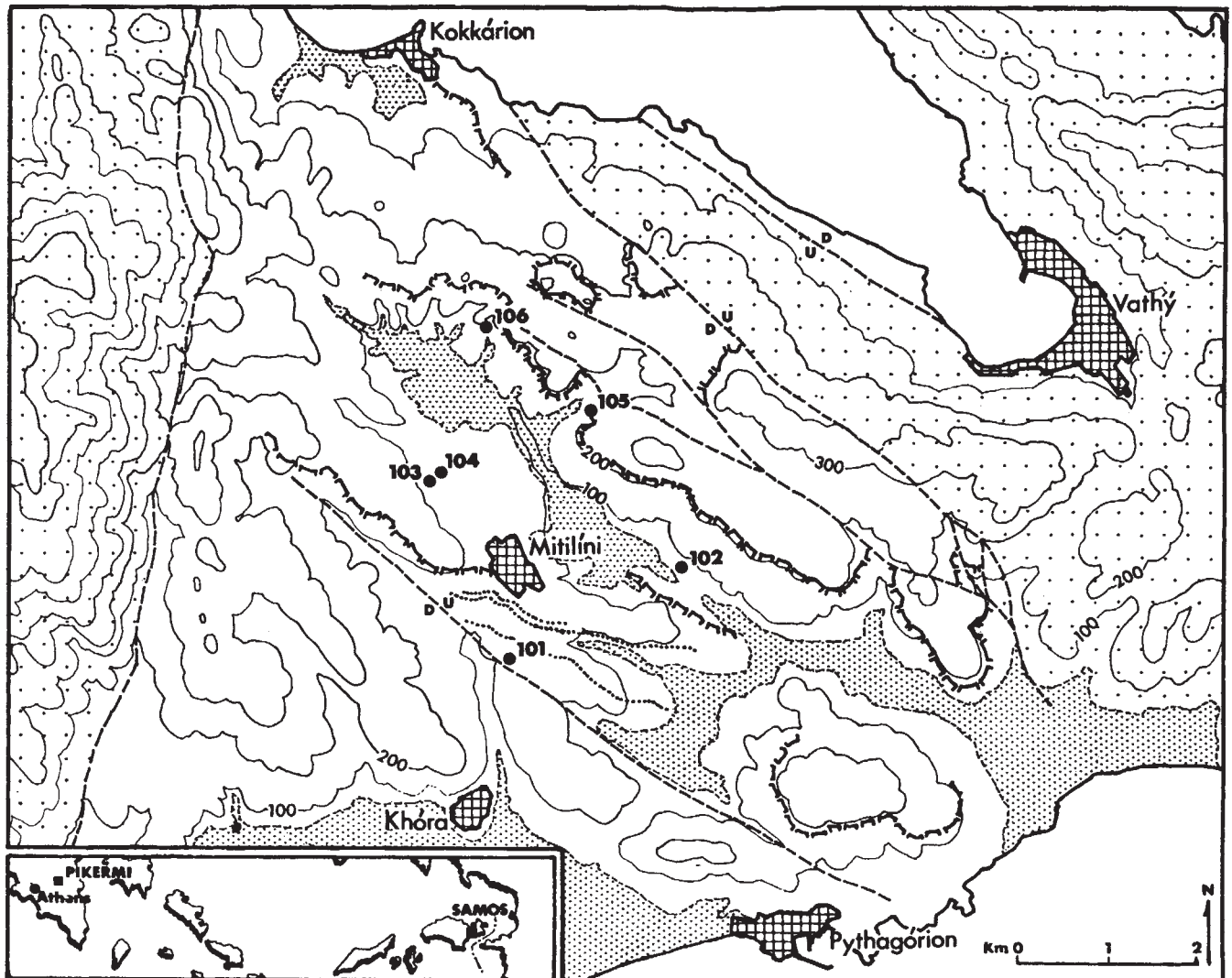


Fig. 1

its base; the relatively young age of GM-103 is invalidated by GM-104, which lies directly above it in the section (Fig. 1) and which has an age similar to the others from this unit. The age of GM-101 is appropriate to its position near the base of unit 1, but there is nothing in the geology of the basin to suggest that the pumice-breccia to which this date refers should be as much as 10 m.y. older than the others. It may be that the slight differences in diagenetic history and in chemistry between GM-106 and the other dated samples make its age suspect, and that a date closer to the rough average of the three "best" dates of unit 3, for example, about 9.3 m.y., should be adopted for the quarry 1-4 fossil bed, but such a decision should await more evidence.

The Samos fauna has long been considered closely comparable with the longer-known and more famous fauna preserved in ancient alluvial fan deposits at Píkermi, near Athens^{8,13}. The difference between the faunas is slight—for example, the hypsodont rhinoceros *Chilotherium*, the caprine *Pachytragus*, and the giraffid *Samotherium* at Samos, or the monkey *Mesopithecus* at Píkermi—and is commonly attributed to slightly more pronounced steppe conditions at Samos rather than a difference in age^{14,15}. The highly steppe-adapted forms which differentiate Samos from Píkermi are also known from local faunas to the east, such as Maragha in Iran and Pavlodar in western Siberia, and in the case of *Samotherium* from localities in North Africa as well¹⁵⁻¹⁷. On the other hand, the faunas which more closely resemble those of Píkermi are found to the north and west, for example, Saloniki in

Macedonia, Veles in south Yugoslavia, and Mount Léberon in France, but are, if anything, less steppe-adapted than Píkermi, so that the picture of a gradational change in biofacies, from Afro-Asian to European conditions in coeval faunas, is easy to see. It is, however, slightly misleading, if no more than that, to group all these in a chronological whole; Sondaar¹⁸ has presented preliminary evidence, based on the biometrics of the Samos hipparions, that the quarry 5 fauna, which seems to be at a higher level, contains equids more like those of Maragha than Píkermi, whereas the opposite is true in the quarry 1-4 assemblage. More advanced forms of *Pachytragus* (personal communication from A. W. Gentry) and of the armadillo *Orycteropus* (personal communication from P. Y. Sondaar) are also said to occur in the quarry 5 assemblage, which would confirm the indication of a significantly younger age for this fauna and perhaps for Maragha and similar "oriental" faunas as well.

On the other hand, forest-adapted *Hipparion* faunas more primitive than that of Píkermi, in that they include both precursor-types to the highly steppe-adapted forms and also numerous survivors from even earlier forest faunas, are well known in Spain, where they characterize the Vallesian "stage" of Crusafont¹⁹; they are palaeontologically and stratigraphically older than steppe-adapted *Hipparion* faunas only a little different from those of Píkermi, with which Crusafont has identified the Turolian "stage"²⁰. Both these intervals endured long enough to encompass marked evolutionary changes in local populations of small mammals²¹⁻²³. Likewise in

MICROPLANKTON ZONE CALIBRATION			EUROPEAN "STANDARD" STAGES/AGES		EUROPEAN K-Ar DATES ← Marine Continental →	EUROPEAN + N.AFRICAN VERTEBRATE FAUNAS <i>Dated - Compared</i>	EUROPEAN LAND MAMMAL AGES
<i>Berggren</i>	<i>modified</i>						
	m.y.		ZANCLIAN			<i>Perpignan, Nîmes, Weze</i>	"ASTIAN"
N 18	5	N 18					
N 17	6	N 17	MESSINIAN	← Ischia		<i>Alcoy</i>	
				← Melilla sup.		<i>Arquillo</i>	
	7						
	8			← Elba	Guilliz →	<i>Melka el Ouidane, Samos 5,</i>	
N 16				← Melilla moyen		<i>Los Mansuetos, Maragha,</i>	
				← Melilla inf.		<i>Baltavar</i>	TUROLIAN
	9	N 16			SAMOS →	<i>Samos 1-4, Pikermi,</i>	
					→	<i>Mt. Léberon, Polgárdi</i>	
	10		TORTONIAN				
N 15							("Pontian")
N 14	11			← Arroudjaoud		<i>Sebastopol, Beni Mellal,</i>	
				Stará Kremnička		<i>Can Llobateres, Csakvar</i>	VALLESIAN
N 13	12	N 15				<i>Odessa, Nombrevilla,</i>	
N 12		↑			Höwenegg →	<i>Baccinello 3, Bou Hanifia</i>	
N 11		N 14			Hohenstoffeln	<i>Höwenegg, Eppelsheim</i>	Hipparion
N 10	13					<i>Öhningen, Baccinello 1-2,</i>	
				← Horsá, Brhlovce		<i>St. Gaudens, Devínská N. Ves</i>	MAREMMIAN
N 9		N 13		← Százice			("Sarmatian")
	14		SERRAVALLIAN		Heilsberg →	<i>La Grive, Manchones, Can</i>	
				← perlite		<i>Mata, Göriach, Chios</i>	
N 8		N 12		← Jungkernbühl	→		"VINDOBONIAN"

Fig. 2

Turkey, Özansöy²⁴ has described at least two "infra-Pikermien" *Hipparion* faunas, and there seems little reason to doubt that *Hipparion* itself appeared in the Mediterranean basin well before the time of the Pikermi and Samos faunas. The immediately pre-Hipparion "phase" of land mammal history, usually called "Sarmatian", has been termed Maremmian by Lorenz²⁵. In their method of definition and use, the Maremmian, Vallesian, and Turolian are not stages, but are similar in all ways to the divisions of geological time called Land Mammal Ages in North America¹.

Radiometric studies in Europe and North Africa confirm the suggestion of Evernden and his colleagues¹ that *Hipparion* first appeared in the Mediterranean basin about 12 m.y. ago, about the same time that the genus evolved in Early Clarendonian faunas of North America. In Morocco, the Melilla tuffs (Fig. 2) unconformably overlie sharply folded normal marine "marnes bleues", and are dated from approximately 8 to 6.6 m.y. in ascending order²⁶. At Bou Hanifia (Oued el Hammam) in Algeria, marine strata correlated with the "marnes bleues" are underlain by beds with a well known *Hipparion* fauna which has Vallesian affinities^{17,27}. Inasmuch as the "marnes bleues" may be at least partly older than the syntectonic Arroudjaoud granite in Algeria, dated about 11.1 m.y.²⁶, the evidence in North Africa suggests an early *Hipparion* fauna dating from at least 12 m.y. ago.

Tobien *et al.*²⁸ have excavated a primitive, forest-adapted *Hipparion* fauna, resembling that of Eppelsheim¹⁵, from tuffaceous and limnic beds on the flank of the Höwenegg

volcanic centre in southern Germany. The geology is controversially interpreted^{29,30}, but the first date on the lava core of the feature of about 6 m.y.³¹ was considered to be too young to apply to the mammalian fauna³². Later Lippolt *et al.*³³ dated hornblende lapilli in the base of the fossil bed at 12.4 m.y. (Fig. 2), and considered this age to be more in accord with the geology.

The Süßwassermolasse in Switzerland and southern Germany contains a well known "Sarmatian" vertebrate fauna, typified at Öhningen, which represents a population immediately before the arrival of *Hipparion*¹⁵. The Süßwassermolasse is underlain by the Deckentuffe, dated at 14.0 m.y. at Heilsberg and 14.2 m.y. at Jungkernbühl; its uppermost member, the Jüngere Juranagelfluh, is overlain by bentonite dated 12.5 m.y. at Hohenstoffeln, and by the Höwenegg hornblende-tuff dated 12.4 m.y.^{30,33}. From this we may conclude that central European mammalian faunas did not yet contain *Hipparion* at ages as young as 13 m.y., and set an arbitrary date for its arrival of 12.5 m.y.

In 1865, Lyell³⁴ agreed to include among Pliocene molluscan faunas, according to his well known statistical method the, brackish-marine assemblages collected from the Aralo-Caspian Formation, a sequence of limey beds also known to contemporaries as the Steppe Limestone, Calcaire d'Odessa, or Pontian Formation, traceable from the north shore of the Black Sea through the Caspian, Aral, and Azov basins; a little later exposures of these beds in the Crimea were made the type of the Pontian Stage³⁵. In 1929, Matthew³⁶ suggested

that the appearance of *Hipparion* was nearly synchronous in North America, India and Europe; pointing to the occurrence of a relatively primitive *Hipparion* fauna in the lower part of the stratotype Pontian at Sebastopol, he argued that the first appearance of *Hipparion* could thus be used to define the base of the Pliocene in continental mammalian successions. In this way, "early Pliocene" and "Pontian" became equivalent terms in vertebrate biostratigraphy.

Long before this, however, the correlation of the largely endemic Pontian molluscan fauna to that of the Mediterranean Pliocene had raised difficulties. These probably began with Gaudry³⁷, who was forced to explain the close association of Pontian molluscs with the Pikermi local fauna by arguing that the mammals, at that time accepted as Miocene³⁴, had been driven from the plains below to starve on the marble slopes of the Pentelic Mountains, and eventually to be entombed by an encroaching Pliocene inundation. It had come to be widely questioned whether the lower part, at least, of the original Pontian Stage should not be placed in the Upper Miocene³⁸. Nevertheless, Matthew's suggestion was quickly taken up by influential vertebrate palaeontologists^{39,40}, although one⁴¹ felt it necessary (*pace* Gaudry) to propose that the association of mollusc and mammal fossils at Sebastopol, similar to that at Pikermi, was formed because Pliocene mammals fell into fissures in Upper Miocene limestone. Since then, although the Miocene age of the original Lower Pontian (now referred to Upper Sarmatian and Maeotian, beneath Pannonian or "Pontian *sensu stricto*") is less than ever in doubt⁴², and its correlation to the Greek "Pontian" with the Samos and Pikermi horizons in the upper part has been substantiated^{15,16,35}, the idea of the *Hipparion* datum at the base of the Pliocene is firmly fixed. Arguments to the contrary⁴³ have been greatly weakened by the obvious ambiguities in conventional marine biostratigraphy in the Mediterranean basin⁴⁴, but we feel that there are enough new data to settle the matter beyond question.

In 1865, Lyell³⁴ reiterated that "... the reader must bear in mind that the terms Eocene, Miocene, and Pliocene were originally invented with reference purely to conchological data, and in that sense have always been and are still used by me" (page 187). Although he did not specify a boundary between the Miocene and Pliocene, one is implicit in northern Italy where a regional unconformity separates strata containing numerous normal marine molluscan faunas which Lyell identified as Miocene, from overlying strata which in the same way can be considered as paratypical Pliocene. In the upper Po Valley, marine formations thus defined as Miocene include the stratotypes, in ascending order, of the stages (except the Zanclean) shown in Fig. 2; the uppermost Miocene interval, missing in this region, is represented in southern Italy by brackish and evaporite sequences⁴⁵, which are thought to have been deposited during a low-water phase when the Tethys was cut off from the open ocean⁴⁶. The succeeding Pliocene faunas indicate a return to normal connexions with the Atlantic. Cita and Blow⁴⁷ compared the microplanktonic succession in these stratotypes with that of the tropical zonation scheme⁵, which allows calibration data obtained elsewhere to be introduced into European chronostratigraphy with greatly improved accuracy and relevance.

At first, the radiometric age of the upper limit of the Messinian Stage, and thus the (approximate) Miocene/Pliocene boundary⁴⁷, was estimated at about 7 m.y. from dates obtained in the Mount Capanne intrusive complex of the Isle of Elba, fragments from which are incorporated in basal Pliocene gravels⁴⁸, but the dates on (presumably) Late Miocene tuffs of Mellila and Guilliz in Morocco²⁶, on marine tuffs associated with the *Sphaeroidinella* datum and on palaeomagnetic features in deep sea cores⁶, and most recently on the pre-Lower Pliocene green tuffs of Ischia⁴⁹, suggest that this should be revised to something like 5 m.y. Since the *Hipparion* datum is about 12.5 m.y. old, radiometric dating and palaeontological correlations agree that most, if not all, of the "Pontian Stage" to

which Matthew³⁶ referred belongs in the Upper Miocene.

In eastern Europe, the estimate for the age of the *Hipparion* datum is substantiated to a certain extent by a date of 14.2 m.y. reported by Afanass'yev⁵⁰ for "Transcarpathia perlite", said (without biostratigraphic documentation) to be Lower Sarmatian, and by dates on Slovakian volcanics, reported by Konecný and his colleagues⁵¹, which date Sarmatian to Upper Sarmatian levels with ages ranging from 13.6 to 11.2 m.y. (Sazdice, Horsa, Brhlavce, Stará Kremnička), again without much cited biostratigraphic evidence. Taken at face value, nevertheless, these dates for the Sarmatian are in excellent agreement with what should be expected for the interval which includes the base of the original Pontian⁴², and in which the earliest occurrences of *Hipparion* in the Soviet Union is placed⁵².

Testing the Calibrated Sequence

The apparent conflict between the date of the Arroudjaoud granite in Algeria (Fig. 2), said to be "post-Tortonian"²⁶, and the age given to the Tortonian interval in Berggren's⁶ microplanktonic time scale, may be illusory. Marine faunas conventionally assigned to the "Tortonian" in the Maghreb can be as old as the Bolli² *fohsi lobata* zone⁵³, about 12 m.y. in the Berggren scale and also well down in the stratotype of the Serravallian stage⁴⁷. Thus the strata which the granite post-dates may be "Lower Tortonian" in the North African sense but actually Serravallian; on the other hand, higher levels may indeed be involved, but until geological details are published the meaning of this date is uncertain.

An interesting and potentially important relationship between the calibrated sequences of fossil microplankton and land mammals has been mapped in detail by Lorenz²⁵ at Baccinello, in northern Italy. Here, beds with a Sarmatian molluscan fauna and a Maremmian land mammal assemblage including the famous remains of *Oreopithecus bambolii* Gervais (fauna VI 2) are conformably overlain by marine sediments in which a sandstone bed, enclosed in foraminiferal marls, contains abundant remains of an early, forest-adapted *Hipparion* fauna (fauna V3). The sequence is capped by freshwater limestones, and truncated by an angular unconformity on which rest marine middle Lower Pliocene beds. In the microfauna associated with the *Hipparion* bed, Lorenz identified nine planktonic species forming an assemblage which is limited to the interval between zone N.13 and zone N.16, inclusive, by the downward limit of the range of *Globigerina* cf. *parabuloides* Blow, and the upward probable limit of *Globorotalia* (T.) ex gr. *mayeri* Cushman and Ellisor in North Italian biostratigraphy^{5,47}. If Lorenz correctly identified *Globigerinoides ruber* (d'Orbigny) the assemblage should be strictly limited to zone N.16, but if he mistook for it the extremely similar form, *G. subquadratus* Brönniman, the assemblage should be strictly limited to zone N.13. The other species identified are abundant in both Serravallian and Tortonian faunas⁴⁷.

A further interesting feature of the Baccinello faunal sequence arises from the identification of the fossil mouse, *Parapodemus* cf. *vireti* Schaub in the V1-2 fauna, and its descendant *Anthracomys majori* Schaub in the overlying V3 fauna. In Spain, this evolutionary sequence implies an age span from mid-Vallesian to latest Turolian²², but this would mean that the (presumably) pre-*Hipparion* faunas of the Baccinello-Monte Bamboli Maremmian, if not those of Öhningen and other central European "Sarmatian" land mammal faunas to which the former are correlated^{15,25}, were coeval with a well established *Hipparion* fauna in Spain, and furthermore that the primitive, forest-adapted V3 *Hipparion* fauna at Baccinello would have coexisted with the highly steppe-adapted Turolian biofacies of nearby Catalonia. While this is not impossible to imagine, we question whether the small mammal stratigraphy is sufficiently established to warrant such conclusions against the sense of the large mammal record.

Finally, it should be pointed out that our calibration of the European Late Neogene (Fig. 2) is in accord with Berggren's⁶

calibration of the microplanktonic zonation if, on the one hand, the V3 *Hipparion* fauna is an Early Vallesian assemblage associated with zone N.13 microplankton, or if, on the other hand, it is Late Turolian (on small mammal evidence) and is associated with zone N.16 microfauna. A third, and to us preferable alternative, that it is an Early Vallesian faunule, with an age of about 12 m.y., in association with a zone N.16 microfauna, conflicts with Berggren's time scale, but is supported by Slovakian chronostratigraphy^{51,52,54} in which the well dated Sarmatian volcanics, 11.2–13.6 m.y. old, correlate with levels overlying Badenian marine strata, which are characterized by a tropical microplanktonic succession from zone N.8 up to or through zone N.14. This requires a slight revision to Berggren's time scale, such that mid-Miocene values are shifted older by about 2 m.y. (Fig. 2) but such a change is acceptable in view of the somewhat tenuous evidence formerly available⁶.

In the calibrated sequence we have outlined, the development of grassland conditions, presumably due to the poleward expansion of subtropical and tropical climate zones during a thermal rise, reached a maximum in the lands north of the Mediterranean between 9 and 8 m.y. ago when the Samos–Maragha type faunas lived. On the other hand, the low-water, restricted-sea conditions of the terminal Miocene, recorded in the characteristic Messinian facies, reached its maximum in the Mediterranean basin about 6 m.y. ago or less. In the interesting palaeoceanographical model proposed by Bandy⁵⁵, a thermal maximum is indicated in marine conditions during the same 9–8 m.y. periods. This is bracketed by two pronounced cold periods which Bandy dates at about 11 m.y. and between 7 and 5 m.y., both of which agree reasonably well with radiometric limits recently put forward for two pre-Pleistocene glacial episodes in Alaska⁵⁶. Whether or not such glaciations would have a major effect on sea levels, as Bandy *et al.* have suggested they might^{55,57}, it seems worth noting the coincidence of the dating. It is incorrect, however, to associate eustatic lowering during the cold period 11 m.y. ago with the Messinian restricted-sea episode, because the 7 to 5 m.y. cold period is in far better agreement with the age of the Messinian as we now understand it.

In spite of the varying degrees of imprecision and controversy which accompany biostratigraphic and radiometric correlations, it seems that the estimate of 12.5 m.y. for the first appearance of *Hipparion* in the Mediterranean world is in good accord with conclusions that can be drawn from studies in Germany, North Africa, Italy and Eastern Europe. The dates from Samos, rounded off to 9 m.y., refer to the more advanced, distinctly steppe-adapted fauna which is seen, most clearly in Spain, to succeed the earlier, forest-adapted biotope. The correlation of the 12.5 m.y. *Hipparion* datum to Italian marine biostratigraphy is not clear, but evidence from Slovakia indicates that it is near to the base of zone N.16, which would change Berggren's⁶ estimate of the age of this point in the planktonic microfossil calibration about 2 m.y. older.

In this interpretation of Late Miocene chronostratigraphy, at least half of the approximately 11 m.y. time range of the genus *Hipparion*¹⁵ falls earlier than the Miocene/Pliocene boundary, when these epochs are defined with Lyell's meaning in the Italian marine molluscan faunas, because both the local and tropical microplanktonic calibrations agree to an age of less than 6 m.y. for this boundary. Matthew's proposition³⁶, made for the convenience of workers in the Siwaliks, that the appearance of *Hipparion* should mark the beginning of the Pliocene in Eurasian land mammal biochronology is invalid and should be abandoned.

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Electron Echo Experiment: A New Magnetospheric Probe

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This article describes a controlled method of investigating the trapping of particles in the Earth's magnetosphere. Instruments in the separated nose cone of a rocket have been used to detect electromagnetic radiation from electrons injected into the magnetosphere from the rocket and magnetically reflected.

ON August 13, 1970, a sounding rocket (Aerobee 350) carrying a high voltage electron gun, electron detectors and other apparatus was launched from the NASA firing range at Wallops Island, Virginia, to a peak altitude of 348 km. The electron gun injected more than 3,000 pulses of electrons, each lasting 16 ms, into the magnetosphere at pitch angles within 25° of the local 90° mirror angle; the current was 70 mA and the energy 35 to 45 keV. These electrons became trapped in the geomagnetic field and bounced between the mirror point near the rocket and the southern conjugate point (-66° latitude, -87° longitude). They simultaneously drifted eastward across the field lines on a shell of constant McIlwain L parameter (≈ 2.56) because of gradient and curvature forces. This rocket launching is the first in a programme designed to study by controlled means the origin and distribution of the natural trapped radiation in the Earth's magnetosphere and to provide a source of electromagnetic radiation for studying wave-particle interactions.

Objectives

Electromagnetic radiation from the electron pulses was detected by equipment on the separated nose cone of the Aerobee 350 (ref. 1). Recently electron beams were successfully injected from a rocket to produce an artificial aurora in the ionosphere which was then detected by ground-based optical means². Although there are certain basic similarities between this experiment and the electron echo programme, our objectives and techniques are different.

Electrons injected from the rocket gyrate in Larmor orbits about the magnetic field and move upward and away from the rocket along field lines toward the southern conjugate point, either immediately or, if the injection pitch angle was less than 90° , after a preliminary reflexion from the adjacent mirror point under the rocket. If the electron detectors on the rocket are to intercept these electron groups again, the rocket trajectory must be along the drift shell on which the electrons were released and the rocket must have an eastward velocity component in this drift shell which matches the electron gradient and curvature drift velocity. The theoretical and observed

bounce periods and drift velocities appropriate to the present experiment are given in Table 1. It was found possible to direct the Aerobee 350 trajectory in such a way that during a portion of its flight it moved tangent to a drift shell, and with the proper eastward velocity component. On the upward leg of the flight electrons were intercepted for about 1 min after one and sometimes two complete bounces.

Table 1 Parameters of Injected Electrons

	Theoretical						Observed
	No scattering			Scattering at 100 km			
Energy (keV)	35	40	45	35	40	45	
Bounce time (ms)	720	675	645	675	640	605	600-700
Drift distance in one bounce (m)	506	542	577	504	540	575	470-580
Drift velocity (ms ⁻¹)	702	803	895	747	844	950	780-820

Theoretical values are integrations of the equation of motion along a model (GSFC 12/66) field line. "No scattering" refers to particles injected at 90° pitch angle which magnetically mirror at the conjugate altitude (~ 8 km). Scattering at 100 km refers to particles injected at 115° pitch angle which undergo the minimum scattering needed at 100 km to return them to the rocket. Drift velocity is drift distance divided by bounce time.

Neutralization

The electrostatic capacity of the rocket is small ($< 1,000$ pF) and the release of the electrons in a vacuum would result in the charging of the rocket body to a high positive potential in a few hundred μs , thus preventing the beam from escaping to infinity. Part of our work was devoted to the investigation of the neutralization problem; a neutral 1 A argon plasma beam was emitted in an attempt to establish an enhanced conductivity path from the rocket to the ionosphere, and a 9 m diameter conducting disk was centrifugally deployed to increase the neutralization current collection area. The flight timing sequence for these devices is shown in Fig. 1. Electrons with the full beam energy were observed to move freely past the rocket after injection showing that the rocket potential was close to that of the ambient ionosphere. A Faraday cup with programmed retarding voltages was also used to measure the energy of the electrons from the ionosphere which constituted the neutralizing return current. We found that even the bare rocket body (before activation of the other devices) collected enough thermal return current to neutralize the 70 mA electron beam and that the rocket never exceeded the ambient potential by more than 200 V. The field-aligned thermal electron current falling on the skin of the Aerobee rocket (tilted 20° to B) was computed from the observed F_{max} electron

density and should have been about 35 mA; evidently the return current was enhanced above the thermal limit, possibly by a small positive rocket potential. The neutralizing process during beam pulsing shows many interesting features which will not be further discussed here.

less intense than the corresponding first echo and both first and second bounce echoes are much more cleanly resolved in the 1 Hz pulsing mode. The echoes start 620 ± 20 ms after the start of the gun pulse and are detected at the rocket for times between 40 and 90 ms. No third echoes were clearly detected, but at the most favourable flight time for third echoes (when $\Delta L \approx 0$) the gun was operating in the 10 Hz mode and the detectors were swamped with first and second echoes.

Beam Stability

There are theoretical reasons for believing that such highly anisotropic particle streams may be unstable and rapidly thermalize (for example, the two stream instability⁴). A detailed calculation⁵ has been carried out, however, for beams characteristic of the electron echo programme and shows that these should be stable for times of the order of the bounce period. We have shown experimentally that a catastrophic beam loss does not occur within at least two bounce periods. At this stage of the analysis, fractional losses of the beam cannot be excluded. The stability of the beam is consistent with the findings of Cartwright and Kellogg¹ which imply that < 10 mW of the 3,000 W of beam power go into electromagnetic radiation.

If scattering by the atmosphere or particles in the magnetosphere and electric fields or magnetic perturbations are ignored, the electron beams should remain within one Larmor radius (15 m for 40 kV electrons at Wallops Island) of a shell of constant McIlwain L parameter. Because of the non-dipolar components of the geomagnetic field and the variations of the injection pitch angle and mirror points from pulse to pulse, there will be small departures from constancy for L (shell splitting effects) but we neglect these effects in the present analysis. At Wallops Island lines of constant L go approximately 1° north of east and the rocket horizontal velocity was about 15° south of east. The southward rocket motion carried it towards a lower L shell, and its upward motion (before reaching its apogee) toward shells of higher L ; when these effects balanced the rocket remained temporarily on a constant L shell. At the start of the echo period the upward velocity was "too large" and the rocket moved to a slightly higher L shell during the bounce period; at the end of the echo period the upward velocity was diminished and the rocket moved to a slightly lower L shell during a bounce period. The first echoes were seen when the change in L per bounce period was $+6 \times 10^{-5}$ (≈ 6 Larmor radii) and the last echoes when the change in L per bounce was -10×10^{-5} (≈ 10 Larmor radii). Two bounce echoes were seen whenever ΔL per bounce was less than $\approx 3 \times 10^{-5}$. In general, the greater the change in L per bounce, the less intense the echo.

Mirror Heights

The southern mirror heights are about 300 km lower in altitude than the northern mirror heights because of the displacement of the equivalent magnetic dipole from Earth centre. The peak southern mirror point altitude would then be about 50 km and for extreme injection pitch angles would be as much as 300 km below the surface. The echoes are thus undoubtedly due to atmospheric backscattering rather than true magnetic mirroring. If the electrons scatter at ~ 100 km altitude at the southern mirror point, they will have to scatter through a pitch angle change of 25° or more to mirror at or below the rocket altitude in the north and be detected. As the electrons spend a large proportion of time near their mirror points, any backscattering will tend to shorten the bounce period (to as little as 600 ms) in good agreement with the observed value of 620 ± 20 ms. If the electrons are scattered at the mirror points in a north-south direction they will diffuse from the injection L shell to nearby shells. The

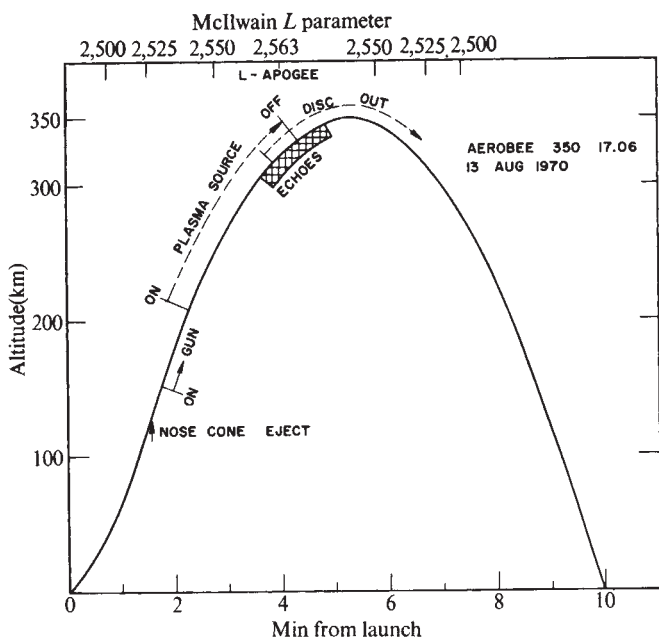


Fig. 1 A plot of the rocket trajectory showing timing of the flight events. Pulses were detected returning from the southern hemisphere during the cross hatched interval. This is approximately the apogee of the rocket in L -space, as indicated by the top scale.

Pulse Sequence

The electron gun sequence was started at 150 km altitude (Fig. 1) and pulsed at 10 Hz for 12 s and then at 1 Hz for 6 s. Each pulse lasted 16 ms and a sawtooth voltage profile was applied which varied between 35 and 45 kV each ms. The beam was injected perpendicular to the rocket roll axis, but covered an angular width of about 10° in electron pitch angle to B and about 1° in a direction around the rocket roll axis. As the rocket spun and coned a $\pm 25^\circ$ range of pitch angles around 90° was thus covered by the gun. Two scintillation detectors and a surface barrier solid state detector with collimated apertures and energy resolution of ± 5 kV were used for beam detection³. Fig. 2 shows a portion of the detector records near the end of and following the 10 Hz mode during a time when echoes from the conjugate points were observed. During each gun pulse the detectors are usually saturated by electrons scattered or spiralling near the rocket. When the gun pitch angle is $< 90^\circ$ the beam is injected downwards and there is an additional response, with a delay of up to 25 ms after injection, to electrons which are reflected from the mirror point directly below the rocket; the injection at A is an example of this. After the 10 Hz pulsing, there is a continuing train of detected echoes, and the behaviour is similar to the response of a delay line on which signals have been stored. The signals which we detected are the particle bunches returning successively from the southern hemisphere conjugate point and the "delay line" is the geomagnetic field line between Wallops and the conjugate point—the observed echo intensities depend strongly on the detector pitch angle and azimuth. Fluxes for the first bounce echoes range from 10^2 to 10^8 electrons $\text{cm}^{-2} \text{s}^{-1} \text{sterad}^{-1}$ and for second bounce echoes up to 10^5 electrons $\text{cm}^{-2} \text{s}^{-1} \text{sterad}^{-1}$ are detected. Second echoes were always

observations of L shell spreading to both higher and lower values are consistent with such diffusion.

The returning beam is appreciably dispersed in the east-west direction by the finite energy spread of the injected beam and the increase of gradient and curvature drift velocity with energy. The rocket will detect only those particles with a drift velocity which matches the component of the rocket velocity in the drift shell. The energy dispersion spreads the beam in the east-west direction to ~ 70 m (5 Larmor radii) in one complete bounce. But if east-west coulomb scattering is as great as the observed north-south scattering (10 Larmor radii), it will obscure the drift velocity-energy relation.

preliminary experiment. The apparent absence of electric fields may be consistent with the low value of $K_p(1+)$ during the rocket flight.

We have demonstrated the feasibility of injecting artificial electron beams of well known characteristics and with measured fluxes comparable with the natural trapped radiation from a rocket into the magnetosphere. Accurate tests of the motion of particles in the geomagnetic field as predicted by the guiding centre approximation of Alfvén can now be made, and both the magnetic field geometry and the presence of electric fields can be investigated with considerable sensitivity. The direct study of wave-particle interactions also is possible, and it

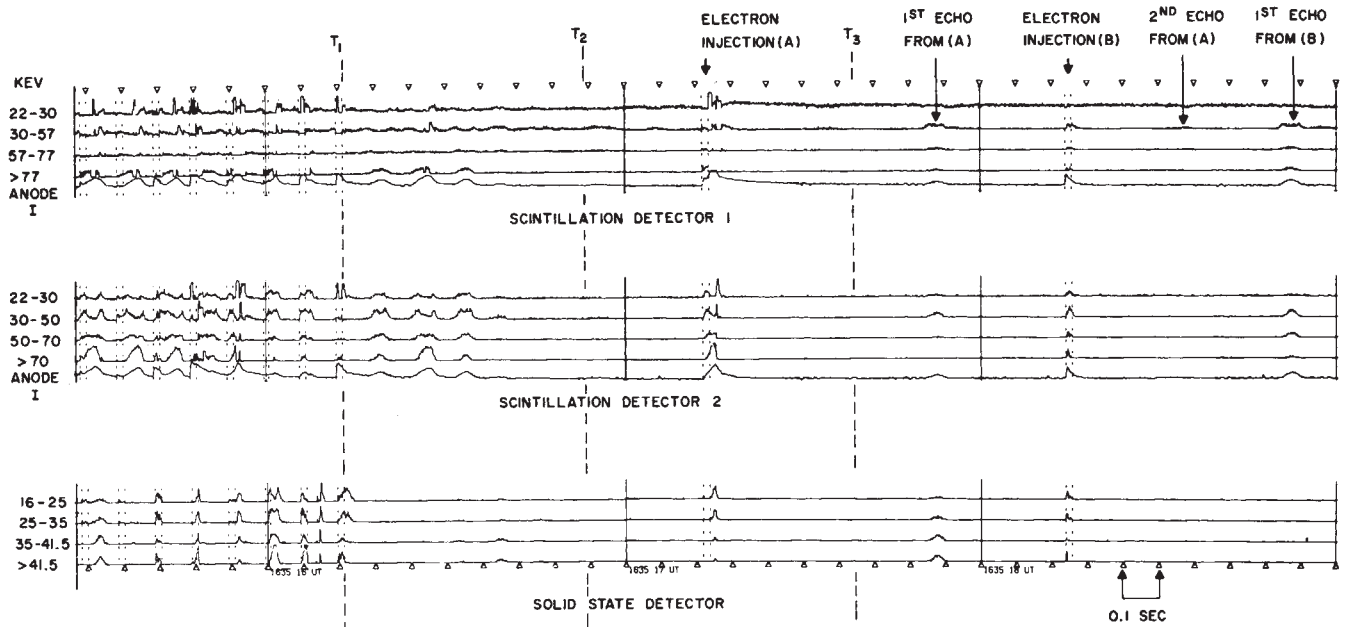


Fig. 2 A sample of electron detector data (3.5 s). The pairs of dashed vertical lines on the data bracket gun pulse intervals. T_1 marks the end of the 10 s gun pulsing rate and the beginning of the 1 s rate. Before the time T_1 the detectors respond to a mixture of injections and echoes from previous injections. From T_1 to T_2 they are responding to mixed first and second echoes from the 10 s mode injections. From T_2 to T_3 , except for injection A, the detectors (primarily the 30–57 keV channel of detector 1) respond to second echoes from the 10 s mode. The 1 s mode injections and echoes A and B are individually labelled and more clearly resolved. Scintillation detectors 1 and 2 and the solid state detector have geometric factors of 4.25, 0.166 and 0.009 cm² sterad respectively; they face perpendicular to the rocket spin axis, with the solid state detector facing opposite to the scintillation detectors. The log of the anode current is plotted (a 5 decade range); the long current decay time constant after a large response is instrumental, and pile-up into higher energy channels in the scintillation detectors is common occurrence because of high fluxes in the events shown.

When echoes were observed eastward velocity component of the rocket in the drift shell varied from 780 to 820 m s⁻¹, well within the theoretical drift velocity range (see Table 1). There was no shift of the electron energy out of the 35 to 45 keV range (within the ± 5 keV resolution of the detectors).

Electric fields perpendicular to the magnetic field produce a drift velocity $|V_d| = |E|/|B|$ in the $E \times B$ direction. If particle drift shells are equipotentials then E is radial at the equator and V_d is east or west (depending on the sign of E), and adds to the curvature and gradient drift. If $V_d \geq 100$ m s⁻¹ (averaged over one bounce) the electrons would drift either too fast or too slow to match velocity of the rocket. Thus the actual detection of echoes implies $|E| < 700 \mu V m^{-1}$ at the equator.

An east-west electric field produces a radial drift. We have seen electron echoes at values of L both higher and lower than the L value at injection, and so there is no evidence for a significant east-west field.

Magnetic field-aligned electric fields produce no drift but do increase the bounce time. The large scattering assumed at the southern conjugate point probably means that the effects of such electric fields would be completely masked in this

is to be expected that such experiments performed at higher geomagnetic latitudes and during geomagnetically disturbed periods will identify, on a cause-effect basis, processes important for accelerating high energy particles.

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Determining Effect of Growth Medium on the Shape and Position of Daughter Chromosomes and on Sporulation in *Bacillus subtilis*

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The nature of the growth medium determines both the packing and the position of the chromosomes and this in turn apparently determines whether the cells will grow or sporulate.

It was commonly accepted that bacterial cultures sporulate only when the growth medium is exhausted. Schaeffer and his colleagues¹ have shown, however, that in cultures of *Bacillus subtilis* in a variety of media, sporulation does occur to some extent during vegetative growth, and that even in a fairly rich medium there is a certain incidence of spores. This incidence may be as low as 1 in 10⁶, for only in starvation media will it approach 100%. On the basis of these facts sporulation was treated as a probability effect¹. We have experimented with cultures growing in a defined medium in a chemostat, and shown that the incidence of spores in the culture is a function of the growth rate². For example, in a culture with a mean generation time of 7 h, the incidence was 36%, while at maximum growth rate in the same medium the incidence was less than 0.1%. At a particular growth rate in a specified medium there was a definite and reproducible probability that a cell would sporulate. A theoretical treatment of the relationship between growth rate and sporulation incidence has been developed in which induction is treated as a random event³.

Sensitivity to Induction

We have also shown that when a culture growing with a generation time of 2 h is starved for intermittent periods of 30 min, spore incidence increases in steps and that at each step, the number of spores is about a quarter of the number that would have been produced by continuous starvation². This suggested that there is a sensitive stage in the growth cycle at which sporulation can be induced and that, in each period of starvation, about 25% of the cells would have been in, or could have reached, this state. Furthermore, the genetic studies of Sueoka and his colleagues⁴ led them to conclude that spores of *B. subtilis* 168 contained only completed chromosomes. As a working hypothesis we therefore thought it reasonable to assume that a forked (replicating) chromosome cannot be enclosed in the developing spore and that the sensitive time for spore induction is the moment when the chromosome has just finished replicating. This hypothesis was consistent with the independent autoradiographic studies of Ryter and Aubert⁵.

To test this hypothesis, experiments were done with *B. subtilis* ts-134. This is a thymine-requiring derivative of *B. subtilis* 168 which is temperature-sensitive in initiation of chromosome replication. At the restrictive temperature (45° C) chromosome replication is completed by there is no initiation of further rounds of replication. At the permissive temperature (35° C) chromosome replication and growth proceed normally⁶.

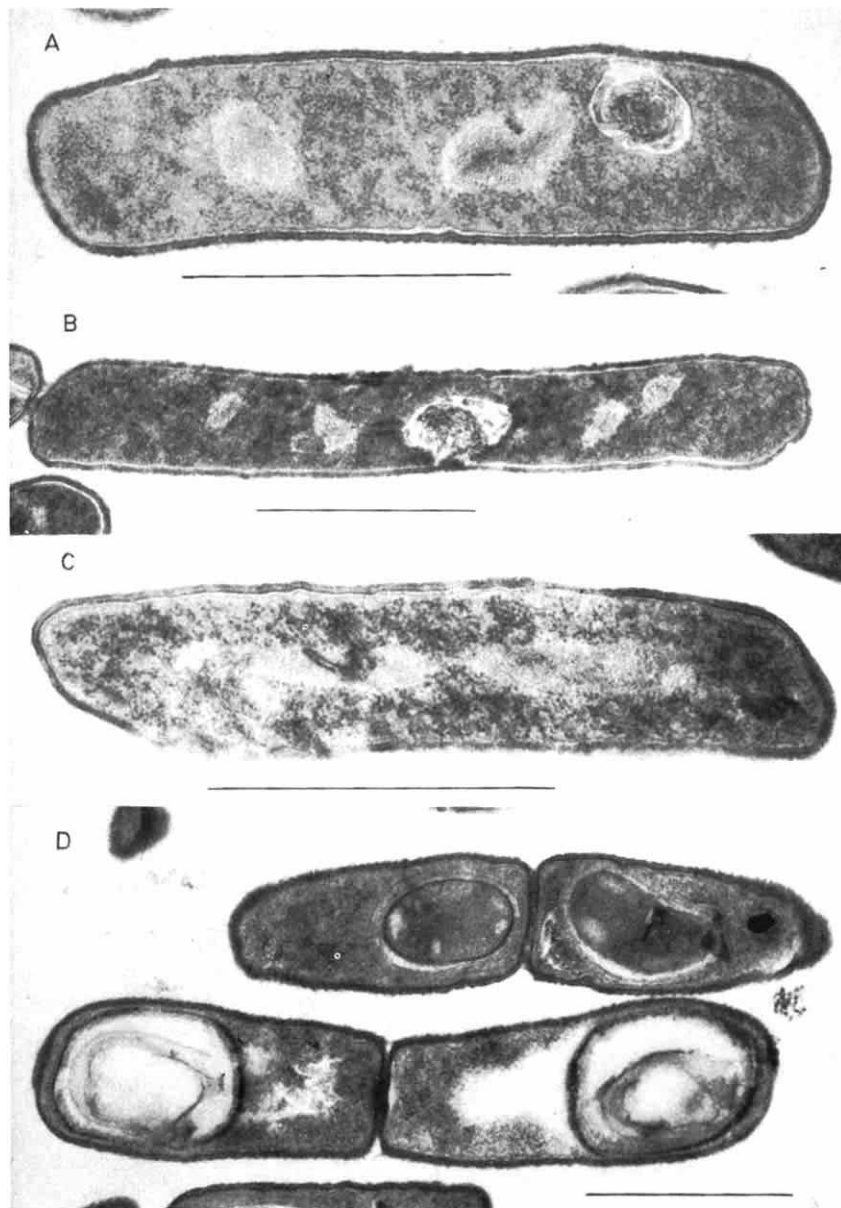
Preliminary experiments were done in which cells were grown at 35° C to mid-exponential phase in a rich (hydrolysed casein) medium containing thymidine. The culture was

transferred to 45° C for 45 min to allow DNA synthesis to be completed, this being checked by analysis of samples taken at intervals. The culture was centrifuged, and the cells resuspended in a poor medium⁷ (glutamate and inorganic ions) in which sporulation is induced but cells do not grow until after a very long period of adaptation. Two portions of the suspension were incubated at 35° C, one with and the other without thymidine. We expected that because chromosome replication had finished, sporulation would proceed equally well whether thymidine was present or not, but the culture incubated without the nucleoside produced virtually no spores (less than 0.2%), and even when thymidine was present sporulation was poor (usually not more than 1–2%) and occurred only after an unduly long period of incubation. Growth experiments and viability measurements gave no indication that failure to sporulate was the result of cell damage produced by exposure to the high temperature. Since the cells were apparently healthy an alternative explanation had to be sought for the fact that the ability to sporulate had been almost entirely abolished. One possibility is that sporulation has to be induced by starvation before chromosome replication is complete and that if it is not, the cells are committed to another round of vegetative growth.

To test this idea cells were again grown to mid-exponential phase in the rich medium with thymidine. The culture was centrifuged and the cells resuspended in two portions, the first in more of the same medium and the second in a poor medium (glutamate and inorganic salts). Both media contained thymidine, and the suspensions were shaken at 45° C for 45 min. In both, the DNA increased by 40%. Both suspensions were centrifuged and, to induce sporulation, the cells were resuspended in poor medium, this time without thymidine. The suspensions were incubated at the permissive temperature and examined in the phase contrast microscope at intervals up to 10 h for development of spores. As before, the cells which had completed their chromosomes in rich medium produced no spores, but of those that had completed their chromosomes in poor medium, 10–20% sporulated. (This value, although low compared with that obtained in *B. subtilis* 168, was similar to that of the control culture not subjected to the high temperature. No reason has been found for the rather poor sporulation in this strain.)

The results support the idea that, if sporulation is to be induced, the starvation stimulus has to be applied while the DNA is still replicating and that if once replication has gone to completion in a rich medium the cells are committed to a further round of vegetative growth and division. This conclusion was confirmed by the appearance of the cells in the electron microscope towards the end of the 45 min period at the high temperature. In those which had completed DNA synthesis in rich medium the chromosomes appeared as white tightly-packed "nucleoids" resembling the chromosomes seen in cells taken from a culture in normal exponential growth (Fig. 1A and B). When replication had been completed in poor medium, the DNA was seen as a diffuse white filament extending along most of the length of the cell (Fig. 1C). This is the appearance that is typically described as stage I of sporulation, in which the two chromosomes of the cell transiently form a single band. Thus it seems that even after 35 min at the higher temperature, that is, by the time that chromosomes replication

Fig. 1 *A*, Cell from culture of *B. subtilis* ts-134 grown at 35° C in rich medium. Two chromosomes appear as tightly packed "nucleoids"; there is also a large mesosome. This is the typical appearance of cells in vegetative growth. The bar represents 1 μ m. *B*, Cell from culture of *B. subtilis* ts-134 grown at 35° C in rich medium, and then at 45° C in the same medium to allow chromosome replication to be completed (see text). The chromosomes present the same tightly packed appearance as in the normal vegetative cell: the mesosome, however, is larger (compare *A*). The bar represents 1 μ m. *C*, Cell from culture of *B. subtilis* ts-134 grown at 35° C in rich medium and then transferred to poor medium at 45° C to allow chromosome replication to be completed. Mesosomes in such cells are small and the chromosomes are extended along the cell to form the axial filament characteristic of stage I of sporulation. The bar represents 1 μ m. *D*, Parallel development of sister cells from a culture of *B. subtilis* 168 (wild type) incubated in poor medium at 35° C for 8 h to induce sporulation. Both pairs of cells show spores which have reached the same stage of development (stage IV and Stage V). The bar represents 1 μ m. See also Table 1.



is just finishing, a large proportion of the cells are already "primed" either for sporulation or for vegetative growth.

These results explain why when cells were subjected to intermittent periods of starvation only a relatively small fraction could be initiated each time. Those that were not initiated were presumably either already committed to another round of vegetative growth or had not yet reached the sensitive phase.

Non-random Sporulation

What remains to be considered is whether these facts are consistent with models in which spore initiation is treated as a random event. If we assume that all cells in a population are likely to sporulate with a given probability, then the chance of finding two specified cells sporulating will be the square of this probability. If it is also specified that they sporulate simultaneously, that is, that they are in the same morphological stage at the same time, the probability is reduced again. *B. subtilis* 168 has a tendency to grow in multicellular filaments consisting of cells which fail to detach after division. This is a useful property because it facilitates the study of the sporulation of sister cells sharing the same micro-environment. Accordingly, comparisons were made of sister cells from two types of culture. The first was a resuspension culture which was sampled 3 and 7 h after the cells had been transferred to the poor medium to induce

sporulation. In such an experiment spores were induced with an asynchrony spread over 2 h or more. At 7 h, when the second sample was taken, about 80% of the cells contained spores in one of the recognizable stages of morphological development of the spore. In the second type of study, continuous cultures were grown in conditions of limiting carbon and containing about 45% of sporulating cells while the rest were in the vegetative stage².

On the assumption that all cells in the culture are equally liable to initiation, the probability of finding two adjacent sister cells undergoing sporulation in the continuous culture is $(0.45)^2 = 0.22$. Moreover, the probability that they will both be at the same stage is less by about a sixth since there are six stages spread over a period of 6–8 h. The observed frequency was, however, 0.9 (Table 1, last line). Because this value is more than twenty times that predicted for random initiation, it seems that sister cells do not behave as random members of the population. Similar calculations can be made from the other values in Table 1 and again these are inconsistent with those predicted on the hypothesis that sporulation in sister cells is initiated randomly. The normal situation, at least in *B. subtilis* 168, is that sister cells sporulate simultaneously and that both cells are at the same stage of spore development. Two typical pairs of sister cells are shown in Fig. 2.

The behaviour of sister cells is consistent with either of two assumptions. The first is that the physiological constitutions

inherited from the mother cell are so nearly identical that there is a very high probability that the sisters will be simultaneously, though independently, initiated and that they will subsequently undergo sporulation synchronously. The alternative explanation is that sporulation is initiated in the mother cell and that the daughter cells are merely continuing a sequence of events that had begun before their "birth". If the second assumption is valid, cell division should take place after sporulation has been initiated, that is, after the cells have been transferred from the rich to the poor medium. Measurements were therefore made of cell numbers and of cell sizes for the first 2 h after suspension in the induction medium. It was found that during this period the number of cells doubled while their length roughly halved, that is, cell division occurred although there was relatively little net synthesis of cell material (Fig. 2). This observation seems to explain in a satisfactory and simple way the closely parallel behaviour of sister cells.

A Model for Spore Initiation

We are now in a position to propose a model which accounts for the observed relationship between sporulation and the growth cycle, for the inherently random nature of the sporulation process in the population as a whole and, incidentally, for the identical behaviour of sister cells. What follows is an amplification of a model that was outlined by Mandelstam⁸.

We start by supposing that the cells make from the materials of the growth medium some metabolite that is an inhibitor of sporulation, and that the richer the medium the more of it they make. For purposes of this argument we are assuming a negative control mechanism involving an inhibitor the nature of which need not be specified. For example, it could be a protein or a small molecule metabolite which activates a protein or even some other type of macromolecule. The inhibitor must be presumed to act on a receptor molecule or surface which might, for example, be a protein in a specific part of the membrane though it could equally well be a segment of the DNA. For simplicity we assume that each cell has one such receptor and that the reaction with the inhibitor is reversible. On this basis, there is a certain probability, determined by the level of inhibitor that has accumulated, that the receptor will be in a free, uncombined state at any moment. In a poor medium, the level of inhibitor would be so low that in most cells the receptors would be in the free state, but even in a rich medium one would expect a few receptors among those of a large cell population to be in this state. From the data presented here it seems that the time at which a cell is sensitive to initiation is limited to some part of the period during which the chromo-

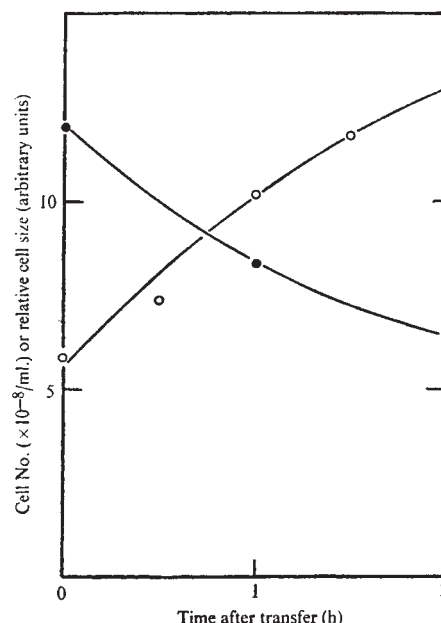


Fig. 2 Changes in cell concentration and size of *B. subtilis* 168 (wild type) after transfer of cells from a rich medium to a poor medium to induce sporulation. Cell concentrations were measured by direct counting, in the phase contrast microscope, of cells plasmolysed by the addition of CsCl and mixed with latex particles (0.5 μ m diameter) to provide an internal standard. The particles were present at 5×10^8 /ml., that is, at about the same concentration as the bacterial cells in the zero time sample. Cells and particles were counted in complete microscope fields until at least 500 particles had been counted. Relative cell sizes were obtained by measuring the length of at least 100 cells seen as complete longitudinal sections in the electron microscope.

some is being replicated. If the receptor happens to be in the uncombined state at this moment sporulation will be induced, but if it is in the combined state induction will not occur. What happens during this period is critical because it determines the position and physical state that the chromosomes will assume as the replication goes to completion. In the uninitiated cell they finish as compact bodies and are positioned for vegetative growth; in the initiated cell they are diffusely spread and the cell is already recognizably in the first stage of spore formation. Whether induction has occurred or not, however, the cell will then divide and its daughters will either sporulate in unison or go through another round of vegetative growth.

In summary, it seems that the nature of the growth medium is a determining factor affecting both the shape and the geographical distribution of the chromosomes that are being formed within the bacillus, and that this in turn determines whether the cell will remain in the vegetative state or whether it will undergo sporulation.

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Table 1 Correlation of Morphological Stages of Sporulation* in Adjacent Sister Cells

Culture	No. of cell pairs	
	Same stage	Different stage
3 h after resuspension†	39	1
7 h after resuspension‡	64	6
Continuous culture§	10	1

* Morphological stages of sporulation⁹ were scored in the electron microscope on thin sections of cells which had been fixed for electron microscopy by the method of Kellenberger, Ryter and Séchaud¹⁰. Only complete longitudinal sections through organisms were considered.

† Resuspension cultures were obtained by growing cells in casein-hydrolysate medium and transferring them at zero time into a glutamate ammonia medium which induces sporulation (see text). 3 h after resuspension, the morphological stages O, II and III of sporulation could be seen.

‡ Seven hours after resuspension all morphological stages between II and VI were observed.

§ The continuous culture samples were prepared and the data obtained as described previously¹¹. In the continuous culture only sisters showing sporulation in either or both cells were scored. The counts of sisters are low since most organisms in chemostat cultures were unicellular.

Mechanism of DNA Replication

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Bacterial cells seem to differentiate between thymine and thymidine, using them separately for replication and repair synthesis respectively. These two processes thus seem to draw their precursors from separate pools.

OKAZAKI'S observation that short pulses of ^3H -thymidine are incorporated almost exclusively into short polynucleotide chains, which only later are joined to long DNA, gave rise to the widely held belief that DNA synthesis is discontinuous and that this is how the two antiparallel chains of the double helix can be copied at the growing point by an enzyme which can only elongate chains in the $5' \rightarrow 3'$ direction¹. Subsequent work on the synthesis and properties of Okazaki pieces has revealed two significant paradoxes. First, clearly more than half the label incorporated by a bacterium such as *Bacillus subtilis*, during a very short pulse of tritiated thymidine, is found in small pieces, yet the same pieces have been reported to be complementary to only one of the two parental chains² and so, if both parental chains are being copied at the same rate, should not have received more than half the incorporated label. The second paradox concerns the number of pieces at each growing point: when the number is calculated from the relation between the overall rate of incorporation of label and the maximum amount of label that can be found in short pieces (unpublished calculations) or from comparing the time required for pieces to accumulate with the rate at which the replication fork progresses³, it seems that there must be very few pieces per growing point engaged in DNA synthesis; however, if calculated from the step time for the creation of TMP residues in DNA, it seems that the chain growth rate is so much less than the rate of movement of the growing point that there must be many growing pieces at each point (personal communication from M. Deutscher).

All published experiments on the labelling of Okazaki pieces have used labelled thymidine because thymidine is quickly incorporated into DNA by wild-type cells and is apparently a preferred source of DNA-TMP for thymine-requiring cells growing in the presence of thymine. In spite of the preference for thymidine, the incorporation of thymine is not affected by the presence of thymidine. It seems, therefore, that thymidine is incorporated into DNA with unusual directness, and its incorporation may not be representative of normal DNA synthesis. For this reason I have studied the labelling of Okazaki pieces in steady state conditions, where a thymine-dependent bacterium growing in the presence of thymine receives tritiated thymine. The results differ from those of labelling with ^3H -thymidine and lead to a new model for the relationship between Okazaki pieces and DNA synthesis. In this model the creation of Okazaki pieces are an event that follows, rather than accompanies, replication and the general synthesis of DNA and the completion of Okazaki pieces before their sealing

are regarded as occurring by distinct mechanisms; and the model resolves the paradoxes mentioned earlier.

Synthesis in Steady State Conditions

Unless stated otherwise, the experiments reported here were carried out with *Escherichia coli* strain 15 thy⁻, arg⁻, met⁻, tryp⁻ (*E. coli* TAMT) growing at 14° C in the presence of 5 µg/ml. thymine. In these conditions, *E. coli* TAMT has a generation time of about 400 min⁵.)

To study the kinetics of labelling of large and small DNA, bacteria were pulse-labelled with ^3H -thymine for periods of from 15 s to 10 min. The sedimentation analysis in alkaline sucrose gradients of the labelled DNA shows that thymine, like thymidine, is incorporated into both small and large DNA (Fig. 1). In contrast to thymidine, however, which labels Okazaki pieces preferentially, if not exclusively, less than 50% of the incorporated thymine appears in Okazaki pieces, even after the shortest labelling period. When pulse-labelling for periods between 15 s and 1 min, the presence of cold thymidine has no effect on the distribution of label between large DNA and Okazaki pieces except that the total incorporation of ^3H -thymine into both kinds of DNA is increased by about 100%. (Thymine also labels a large amount of TCA-insoluble material that stays at the top of the gradient. This material is not DNA because of its buoyant density in CsCl; its possible relation to DNA synthesis is still unclear.)

Because shortening the pulse seemed to reduce, rather than increase, the relative amount of label in Okazaki pieces, I labelled bacteria with tritiated thymine for only 10 s. In these conditions only about 20% of the incorporated label was found in Okazaki pieces (Fig. 2A). Furthermore, when cold thymidine was given at the same time, the incorporation of ^3H -thymine into Okazaki pieces was completely suppressed (Fig. 2B). (It was not possible that the presence of Okazaki pieces was obscured by the very large amount of non-sedimenting material at the top of the gradient because, as shown in Fig. 2C, a 20 s pulse of ^3H -thymine given in the same conditions produced the familiar Okazaki peak.) Thymidine gave very different results from thymine; two-thirds of the label incorporated during a 10 s pulse appeared in small DNA pieces (Fig. 2D).

These experiments show that if thymine is used as label, most of the label appears first in large DNA. This immediately suggests that large DNA is the precursor of Okazaki pieces (rather than the other way around), that DNA replication is not discontinuous and that the creation of Okazaki pieces serves some other function. The preferential incorporation of thymidine into Okazaki pieces suggests that thymidine is a specific precursor for the reaction that joins the pieces. This interpretation would explain the fact that, when compared with thymine, the incorporation of thymidine into DNA accounts for only a small fraction of the total DNA synthesis. This preferential incorporation has also been observed by Fuchs and Hanawalt⁵, after a 10 s pulse at 37° C, more than 95% of the incorporated thymine was found associated with the fork, compared with only 20% of the incorporated thymidine.

New Model of Replication

I propose the following model of DNA replication (Fig. 3): DNA is replicated continuously at the fork through simultaneous elongation of both new strands. Although the precise mechanism of this reaction is still obscure, its preference for thymine rather than thymidine indicates that the replication process is fundamentally different from repair synthesis and possibly involves a different precursor pool.

Okazaki pieces are caused by single strand interruptions that are introduced into one of the two new DNA strands by specific nucleases which recognize short nucleotide sequences spaced at about 3,000 nucleotide intervals along the bacterial chromosome. (These enzymes may not distinguish between

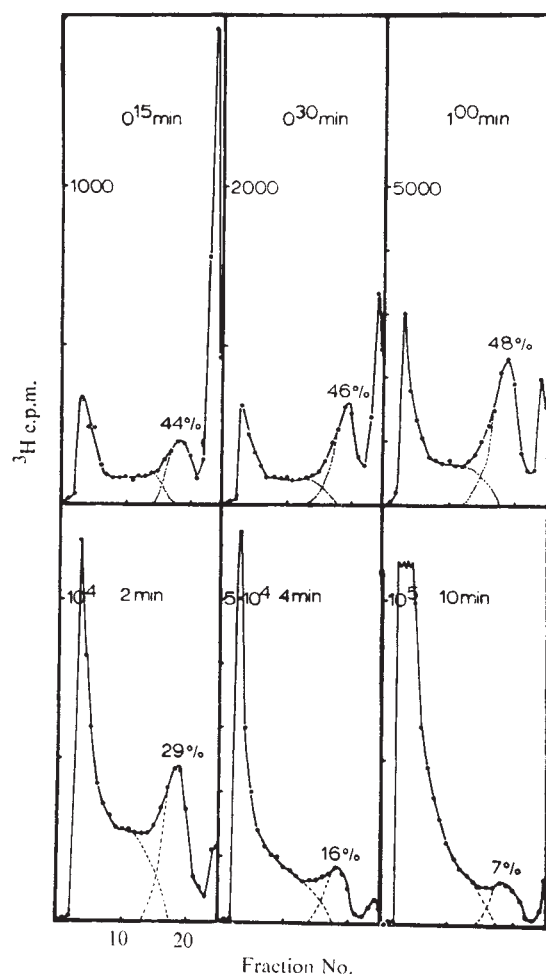


Fig. 1 Sedimentation analysis in alkaline sucrose gradients of DNA isolated from *E. coli* 15 TAMT labelled with ^3H -thymine in steady state conditions. The bacteria were grown for several generations at 14°C in the following medium; 0.01M NaCl, 0.005M KCl, 0.02M NH_4Cl , $6 \times 10^{-4}\text{M}$ KH_2PO_4 , $2 \times 10^{-4}\text{M}$ Na_2SO_4 , 0.001M MgCl_2 , 10^{-4}M CaCl_2 , 10^{-5}M FeCl_3 , 0.02M *N*-tris-(hydroxymethyl) methylglycine (pH 7.4) ('Tricine', Calbiochem) and 0.025M sodium lactate, supplemented with 5 $\mu\text{g}/\text{ml}$. thymine and with 40 $\mu\text{g}/\text{ml}$. each of arginine, methionine and tryptophan. The bacteria were chilled to 0°C under aeration, centrifuged, resuspended in fresh medium at a concentration of 2×10^{10} cells/ml. and stirred in an open beaker at 14°C for 30 min. At time zero, an equal volume of fresh medium was added containing 5 $\mu\text{g}/\text{ml}$. ^3H -thymine (13C/mM). Samples (0.5 ml.) were taken at the indicated times into 2 ml. acetone at -30°C . The cells were centrifuged and resuspended in 1 ml. of 0.3M NaOH-0.1M EDTA. After adding 0.1 ml. 20% 'Sarkosyl-NL 97' (Geigy) the mixture was heated to 65°C for 5 min and then layered on an alkaline sucrose gradient (5-20% sucrose, 0.3M NaOH, 0.01M EDTA, 0.5M NaCl) and centrifuged in a Spinco SW-27 rotor at 26,000 r.p.m. for 16 h. Twenty-four fractions were collected and precipitated with 5% trichloroacetic acid in the presence of some bovine serum albumin.

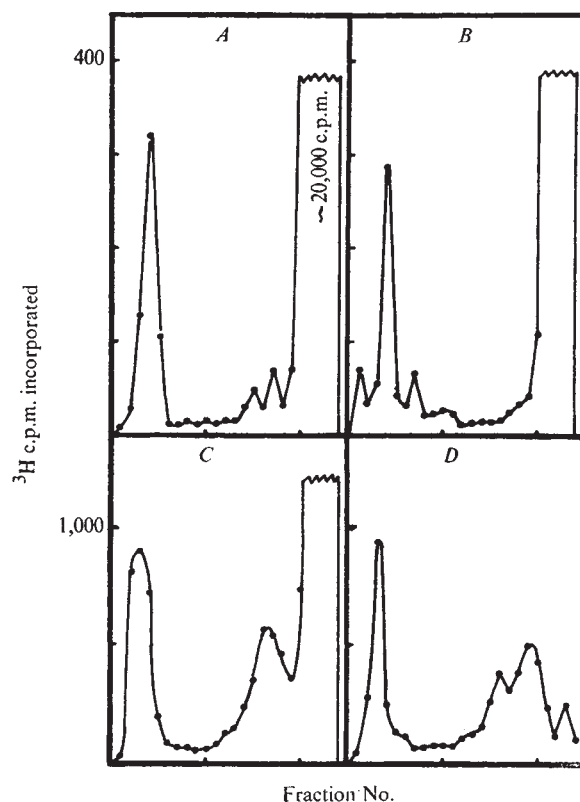


Fig. 2 Sedimentation analysis in alkaline sucrose gradients of DNA labelled under the following conditions: (A) 10 s pulse with ^3H -thymine; (B) 10 s pulse with ^3H -thymine in the presence of 1 $\mu\text{g}/\text{ml}$. cold thymidine; (C) 20 s pulse with ^3H -thymine; (D) 10 s pulse with 0.1 $\mu\text{g}/\text{ml}$. ^3H -thymidine. (Other conditions were as in Fig. 1, except that centrifugation was at 27,000 r.p.m. for 20 h).

parental and new strands and might therefore produce similar nicks in the parental strand of the other daughter duplex.) Thus, the average distance of the first chain interruption from the fork is about 1,500 nucleotides or half the size of an Okazaki piece³. At 14°C the growing point takes 10 s to move along this length of DNA. Therefore, after pulse-labelling with ^3H -thymine for periods longer than 10 s, the amount of label in Okazaki pieces will approach 50%. The average lifetime of the Okazaki pieces at the growing point must be about 1 min because the relative amount of label in large DNA starts to increase after pulse-labelling for longer than 1 min (Fig. 1). During that time the fork travels a distance of 9,000 nucleotides or 3 Okazaki pieces. The number of chain interruptions in the newly synthesized DNA should therefore be four.

Between different bacterial strains and in different growth conditions the number of strand interruptions in the newly synthesized DNA varies. When *E. coli* 15 TAMT is grown in the presence of much higher thymine concentrations (20-50 $\mu\text{g}/\text{ml}$.) and pulse-labelled with either ^3H -thymine or ^{32}P -phosphate, little, if any, label is found in Okazaki pieces. This suggests that the accumulation of strand interruptions in the new DNA results from a relatively slow repair process caused by thymine deficiency and does not occur in normal conditions. (In the same conditions, thymidine is still incorporated into Okazaki pieces, indicating that there may be a second class of pieces not labelled by thymine.)

The mechanism of chain elongation at the growing point is largely unknown but DNA synthesis is probably not discontinuous. Because thymine is found nearly exclusively in large DNA after a very short pulse, it seems possible that the two new DNA strands are covalently linked at the apex (as indicated in Fig. 3), and so elongation of the new DNA strands would then have to occur by insertion of nucleotide pairs at the apex. This system would have the advantage of making the

replication site inaccessible to repair enzymes. (A similar mechanism was proposed by Morgan⁶). We cannot, however, exclude the possibility of two separate growing chains, the small piece engaged in DNA replication at its 5'-end being hidden under the large peak of non-sedimenting radioactive material.

The sealing of the single strand interruptions by polynucleotide ligase is presumably preceded by some repair synthesis. Probably it is this reaction into which thymidine goes preferentially. If so, labelling with ³H-thymidine should allow us to detect whether similar strand interruptions occur in one of the two parental strands. The following experiment shows that this is the case: *E. coli* B/r (autotroph for thymine) was grown for several generations in a "heavy" ¹³C, ¹⁵N-containing medium, transferred to "light" ¹²C, ¹⁴N-medium for about a third of the generation time, and then pulse-labelled with ³H-thymidine for 10 s at 14° C. Large and small DNA were separated by alkaline sucrose gradient sedimentation and banded separately in alkaline CsCl density gradients. Fig. 4 shows that nearly all the thymidine incorporated into both large and small DNA is covalently connected to heavy parental DNA. The slight shift to lighter density of the Okazaki pieces (Fig. 4A) suggests that a large region has been labelled with thymidine. It is possible that the sudden expansion of the TTP pool caused by the addition of thymidine causes a more extensive replacement of nucleotides than normal in the sealing reaction.

We may have to distinguish between two classes of Okazaki pieces, those labelled exclusively with thymidine and those labelled with thymine or thymidine. Fig. 4 shows that most of the Okazaki pieces that are labelled with thymidine come from parental strands. Because *E. coli* B/r, like strain 15 TAMT growing in the presence of 20–50 µg/ml. thymine, probably has no Okazaki pieces at the growing point, most thymidine-labelled Okazaki pieces must arise from other regions of the chromosome. They might well represent cistrons engaged in transcription. The necessity of single strand interruptions for late mRNA synthesis in phage T4-infected *E. coli* was demonstrated by Riva *et al.*⁷. Genes in a circular replicating *E. coli* chromosome could probably not be transcribed into RNA unless similar strand interruptions are introduced at both ends of the cistron, when the DNA helix could rotate through the bulky RNA and protein synthesizing apparatus (rather than vice versa).

In contrast to the Okazaki pieces that are labelled only by thymidine, thymine-labelled pieces arise from new DNA. They can only be detected in thymine-requiring bacteria growing at low concentrations of thymine, and are probably caused by the accumulation of specific interruptions in one of the two new DNA chains. It seems reasonable that these strand interruptions function as swivel points for the rotation of the daughter

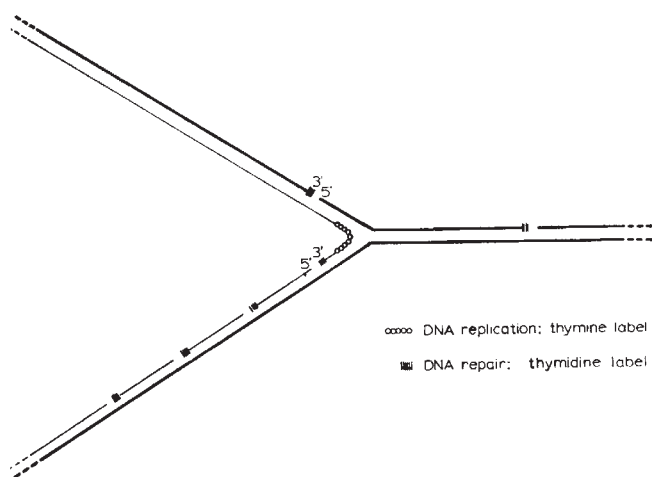


Fig. 3 Model of the structure of replicating fork (explanation in the text).

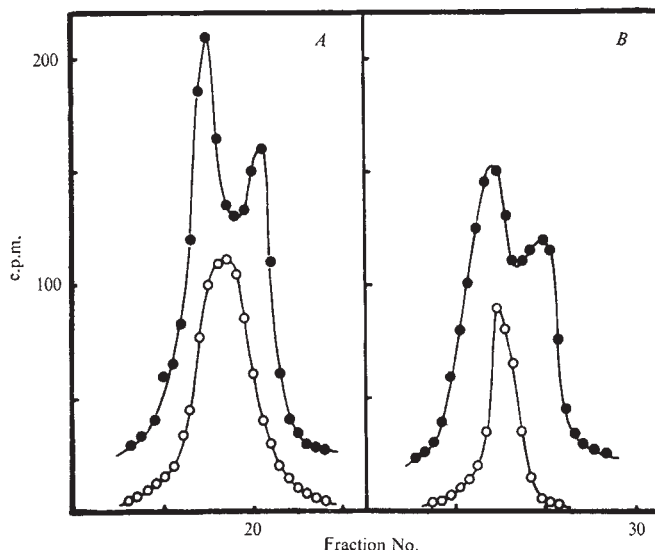


Fig. 4 Density analysis in CsCl of DNA labelled with thymine and thymidine. *E. coli* B/r was grown for several generations in a "heavy" medium containing ¹⁵NH₄Cl and ¹³C-glucose. The cells were washed, resuspended in normal "light" medium (Fig. 1), aerated for 15 min at 37° C, chilled to 0° C, centrifuged and resuspended in fresh "light" medium at a concentration of 10¹⁰ cells/ml. After another 30 min aeration at 14° C, 0.1 µg/ml. of ³H-thymidine was added. The reaction was stopped after 10 s by the addition of an equal volume of cold acetone. After centrifugation and resuspension in Tris-EDTA, the cells were lysed with lysozyme, pronase and 'Sarkosyl', and the DNA sedimented through alkaline sucrose gradients. Fractions containing large and small DNA were pooled, dialysed against 0.05M Tris-0.01M EDTA (pH 7.4), concentrated and banded in CsCl. A, Okazaki pieces; B, large DNA. ○, ³H-label; ●, ¹⁴C-labelled "heavy" and "light" marker DNA.

helices during the replication of the circular chromosome. Similar nicks presumably occur in the parental strand of the other daughter helix. It is even possible that the interruptions in the parental strand are created ahead of the fork, thus providing the necessary swivel point for the unwinding of the parental double helix, and persist throughout the replication region into one daughter helix where they are eventually sealed.

It is still unclear how the cell differentiates between thymine and thymidine using them separately for DNA replication and repair synthesis, respectively. The principal difficulty in understanding this phenomenon is probably caused by our incomplete knowledge of the intermediary metabolism of thymidine nucleotides. We conclude, however, that DNA replication and repair synthesis draw their precursors from separate pools. Whether these pools contain chemically different precursors or whether they are only physically separated remains to be seen. Preliminary experiments on the labelling of the various thymidine nucleotide pools seem to suggest that DNA replication uses precursors different from deoxyribonucleoside triphosphates.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Hekla Eruption Clouds

THE black clouds from the eruption in 1965 of the Icelandic volcano Syrtlingur are reported¹ to have included as a major constituent particles containing high concentrations of heavy metals, supposedly produced by decomposition of the silicates in the magma followed by vaporization and progressive condensation of the decomposition products. The 1970 eruption of Hekla volcano in Iceland provided an opportunity to determine whether this behaviour is a general characteristic of Icelandic volcanic eruptions.

Particles in the Hekla eruption cloud were sampled for 4.5 h on May 9, 1970, from a US Air Weather Service C130 aircraft equipped with "record-changer" filter holders loaded with cellulose (IPC) filters². One large filter (42 cm in diameter) was used during the entire sampling period; additional samples were taken for shorter time periods on smaller filters.

The nature of individual particles was determined with optical and electron microscopy and electron microprobe techniques. Larger particles (> 100 μm in diameter) could be shaken from the filters but smaller particles were removed from a section of the large filter by immersing it in an ultrasonically agitated 'Freon' bath. Other parts of the large filter were analysed for silicon by neutron activation, and for water-soluble constituents by methods described by Cadle *et al.*³.

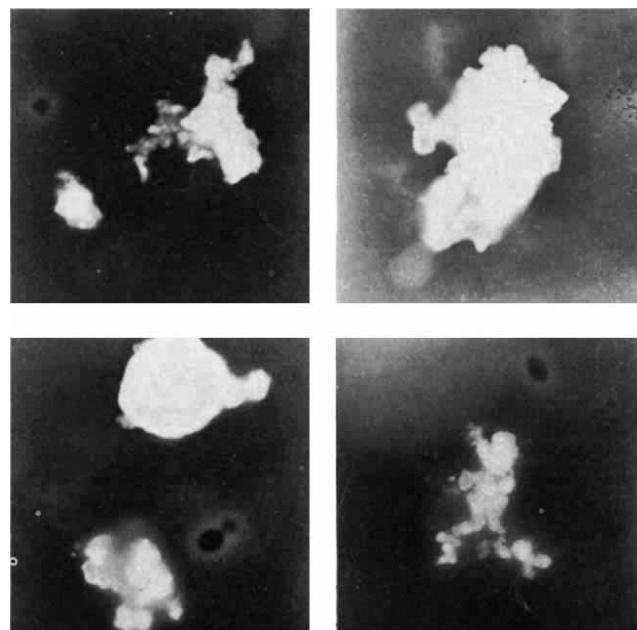


Fig. 2 Electron micrographs of particles collected from the Hekla eruption cloud. Distance across each micrograph is 3.1 μm .

Examination of a large number of the particles with an MAC electron microprobe indicated that almost all of those that could be removed from the filters by ultrasonics were lava. The only exceptions were a few particles that contained unusually high concentrations of calcium. (Droplets in the eruption clouds would not be detected by this technique.) Optical microscopy of the large particles indicated that they were all irregular glassy fragments of lava (Fig. 1). Many of the smaller particles, examined by electron microscopy, consisted of aggregates including some spherules (Fig. 2).

The analytical results are shown in Table 1. The analytical methods were such that only the silicon could have been in a water-insoluble form and it was probably largely part of the lava silicates. Much of the eruption cloud consisted of sulphates and sulphuric acid. The concentration of fluorine corresponds to about 1,600 p.p.m. by weight in the collected particulate material, assuming a silicon concentration in the lava of about 55%⁴. This agrees remarkably well with

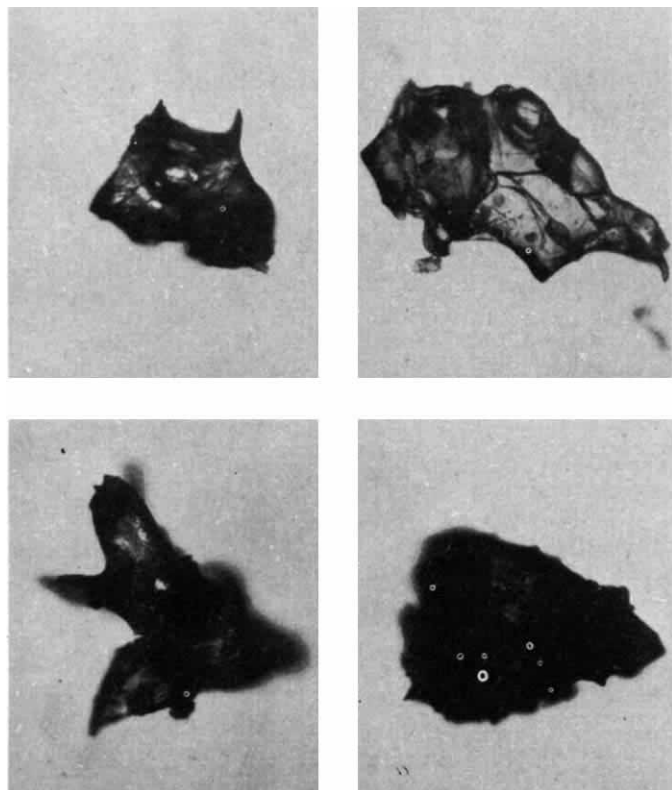


Fig. 1 Photomicrographs of large particles collected from the Hekla eruption cloud. The particles were about 0.1 mm across.

Table 1 Analysis of Particles collected from Hekla Eruption Cloud

Component	Concentration ($\mu\text{g}/\text{m}^3$ ambient air *)
SO_4^{2-}	5.5
Si	9.1
NH_4^+	1.0
Na^+	0.20
K^+	0.063
Mg^{2+}	0.036
Ca^{2+}	0.11
F^-	0.07
Cl^-	0.29

* At 5,000 feet altitude, 3° C.

analyses of the ash (tephra) that deposited on the ground near the eruption vents⁴.

These results agree qualitatively with those obtained for Mayon, Arenal and Kilauea eruptions³, although previously fluorine was not detected. It is possible that particles similar to those observed by McClaine *et al.*¹ were overlooked, but if so they must have constituted a very small fraction of the particles in the eruption cloud. The difference between these results and those obtained by McClaine *et al.*¹ for the Syrtlingur eruption cloud may result from the fact that seawater had access to the Syrtlingur eruption vent. Seawater coming in contact with molten lava may induce partial decomposition.

We thank Evelyn Frank for help in preparing the electron micrographs and Walter Pollock and Bruce Gandrud for neutron activation and chemical analyses.

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Reversals of the Earth's Magnetic Field

Kawai and Hirooka¹ have examined the results of archaeomagnetic observations, and those of secular variation, to investigate the movement of the geomagnetic dipole field during the past 2,000 yr. They found a wobble of the dipole axis around the rotational axis: an idealized model of this quasi-hypotrochoid motion is shown in Fig. 1. The nearest approach to the rotational axis occurs approximately every 500 yr and the greatest deviation of the dipole axis from the rotational axis is $\sim 18^\circ$. Lilley² suggested that such a deviation of the dipole axis is an expression of asymmetric motion in

the Earth's core. Increasing evidence indicates the necessity for asymmetry in core motions if a regenerative dynamo is to be established (for example, see Braginskii³). Nagata⁴ has proposed that this is a mechanism for reversals of the geomagnetic field, the dipole field decaying as the flow pattern approaches symmetry. Lilley's suggestion is that if the dipole axis coincides with the rotational axis it is an indication that the flow in the core is becoming symmetrical and, as a consequence, the dipole field will decay. When the flow pattern again becomes asymmetric, the dipole field will begin to grow once more, perhaps in the opposite direction, and the dipole axis will again wander from the rotational axis.

It is interesting to estimate how close the two axes would have to come to initiate this postulated sequence of events. I will use the probability density function ρ introduced by Fisher⁵ to analyse statistically a set of vectors, and defined as follows: given a small area of size dS on a unit sphere at an angular distance ψ from the mean direction (the pole), the proportion of the total end points expected in dS is ρdS . ρ is given by

$$\rho = C \exp(\kappa \cos \psi) \quad (1)$$

where κ is a constant, called the precision parameter, which describes the tightness of the group of vectors about their mean direction. The constant C is chosen so that

$$\int_S \rho dS = 1 \quad (2)$$

where the integral is taken over the area on the sphere on which end points of the vectors lie. If this is the whole sphere, it is easy to show that $C = \kappa/4\pi \sinh \kappa$. Here, ψ is restricted to values less than $\psi_1 \approx 18^\circ$. From equations (1) and (2)

$$\begin{aligned} 1/C &= \int_S \exp(\kappa \cos \psi) dS \\ &= \int_0^{\psi_1} \exp(\kappa \cos \psi) 2\pi \sin \psi d\psi \end{aligned}$$

Since $\cos \psi_1 \approx \cos 18^\circ \approx 0.95$

$$1/C \approx \frac{2\pi}{\kappa} \{\exp(\kappa) - \exp(0.95\kappa)\} \quad (3)$$

If dS is a small circle ($\psi = \psi_0$) around the pole

$$\begin{aligned} \rho dS &\approx C \exp(\kappa \cos \psi_0/2) 2\pi (1 - \cos \psi_0) \\ &\approx \frac{\kappa (1 - \cos \psi_0)}{1 - \exp(-0.05\kappa)} \end{aligned} \quad (4)$$

The best estimate k of the variable κ is given by⁵

$$k = \frac{N-1}{N-R}$$

where N is the number of vectors and R their resultant. If ψ is restricted to values less than $\psi_1 \approx 18^\circ$, then the minimum value of R is $N \cos 18^\circ$ so that the minimum value of k is

$$\frac{N-1}{N - N \cos 18^\circ} \approx \frac{1}{1 - 0.95} = 20$$

From equation (4)

$$\rho dS \approx \frac{20 (1 - \cos \psi_0)}{1 - \exp(-1)} \approx 32 (1 - \cos \psi_0) \quad (5)$$

The time between nearest approaches of the dipole axis to the rotational axis is ~ 500 yr, so that $\sim 2,000$ near approaches will occur each million years. The number of reversals in recent times is ≈ 3 per million years. It follows from equation (5) that

$$\begin{aligned} (2,000) (32) (1 - \cos \psi_0) &= 3 \\ \text{that is, } \psi_0 &\approx 36' \approx 1/2^\circ \end{aligned}$$

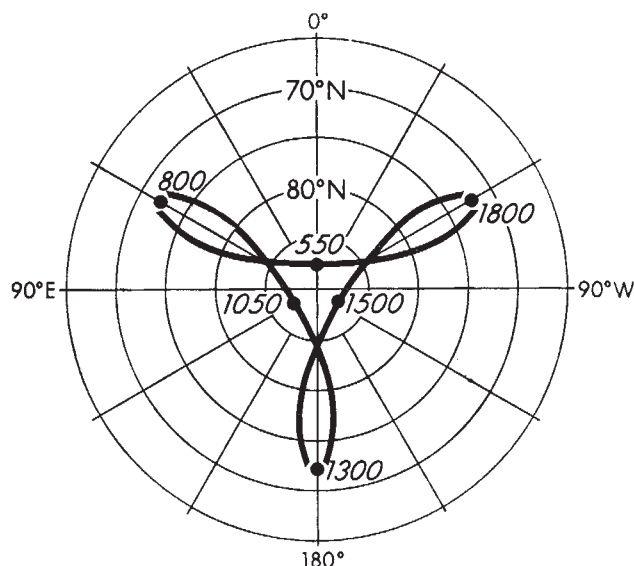


Fig. 1 Model of quasi-hypotrochoid motion of the geomagnetic dipole axis during historic times. Numbers on the curve represent dates in yr AD (after N. Kawai and K. Hirooka¹).

If in approximately only half of the cases when the two axes coincide and the dipole field decays the field builds up again with the same polarity instead of reversing, my estimate of ψ_0 for reversals to occur is modified slightly. It must be stressed that my calculation is based on several hypotheses. If the underlying assumptions are realized in the Earth, then it would seem that if the dipole axis approaches the rotational axis to within about 0.5° , then a reversal of polarity of the Earth's field is likely to occur.

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Polywater on Silica-free Substrates

WE have shown¹ that a form of polywater with a slightly different infrared spectrum from that obtained by Lippincott *et al.*² can form between calcium fluoride optical flats. This led to the conclusion that $-\text{Si}-\text{O}$ groups are not essential for the formation of polywater.

We have attempted to produce polywater by the same process using a variety of water-insoluble substances transparent to infrared radiation. All the materials used were optically flat except spectroscopic grade silver chloride sheet, which was made as flat as possible by compression between glass optical flats.

Experiments using semiconductor grade, single crystal silicon, 'Irtan-2' (sintered polycrystalline zinc sulphide), silver chloride, and fused silica ('Infrasil') gave no detectable product. But after 3 days at 97% relative humidity, magnesium oxide single crystals (99.95% pure, artificially grown periclase (Spicer) became covered with a surface layer of a translucent substance approximately $2\ \mu\text{m}$ thick. The infrared spectrum of this material, both on the periclase surface (Fig. 1) and on a calcium fluoride surface, after transfer by scraping with a barium fluoride crystal, was similar to that of the polywater prepared by Lippincott *et al.*², together with a small proportion of normal water. Magnesium hydroxide gave no such spectrum, nor did a magnesium oxide plate after soaking in liquid water for 3 days.

The magnesium oxide was cleaved along the 100 plane before it was ground and polished: subsequent X-ray diffraction confirmed this assignment of the cleavage plane.

Most of the current models²⁻⁹ for the structure of polywater attempt to accommodate some or all of the following experimental "facts": an assumed density of $1.4\ \text{g cm}^{-3}$ (refs. 2 and 8), an assumed value for the $\text{O} \cdots \text{O}$ spacing at the surface of fused silica of about $0.28\ \text{nm}$ ⁵ and an assumed $\text{O} \cdots \text{O}$ distance of $0.232\ \text{nm}$ in a linear hydrogen bond^{2,6,8,9}, based on Lippincott *et al.*'s interpretation of the infrared spectrum. The experimental data, on which the first two of these values are founded, must be regarded as doubtful. The value for the density is doubtful because of the probable presence of contaminants¹⁰ in the particular samples on which the value has been based¹¹, and fused silica does not have a sufficiently well characterized surface for assignments of interatomic distances to be made with any certainty. The $\text{O} \cdots \text{O}$ distance of $0.232\ \text{nm}$ often assumed has been calculated by Lippincott *et al.* by analogy with the infrared spectrum of FHF^- . It would have been better to have used the correlation of the $\text{O}-\text{H}$ stretching frequency in $\text{O}-\text{H} \cdots \text{O}$ bonds with bond length¹². This gives $0.24\ \text{nm}$ as the bond length of an $\text{O}-\text{H} \cdots \text{O}$ bond absorbing at $1,595\ \text{cm}^{-1}$. This estimate also involves an

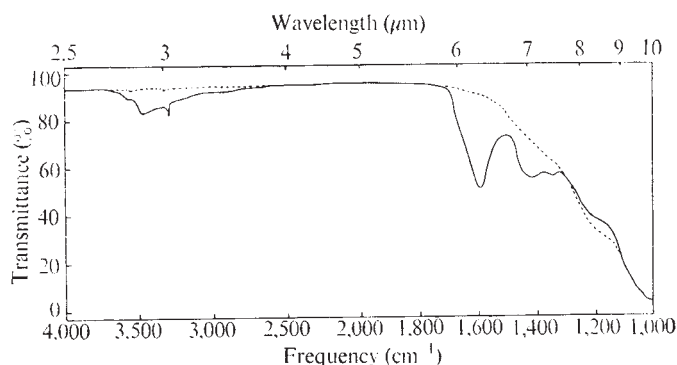


Fig. 1 Solid line, infrared spectrum of polywater formed on MgO (no scale expansion). Dashed line, MgO background.

extrapolation. Thus there has been no sound basis so far for the construction of a model.

In spite of the restricted range of substrates so far examined, it seems that ordered, highly electronegative groups at the substrate surface are essential for the formation of polywater. Magnesium oxide is the only well characterized surface studied so far on which polywater forms with an infrared peak at $1,595\ \text{cm}^{-1}$ and a doublet around $1,400\ \text{cm}^{-1}$ similar to the polywater of Lippincott *et al.* Magnesium oxide has a face centred cubic structure with a unit cell of $0.4212\ \text{nm}$ (ref. 13), so that the closest distance between oxygen atoms is $0.298\ \text{nm}$. Any model proposed to explain the infrared spectrum of Lippincott *et al.*'s polywater, which assumes that the surface acts as a template, must agree with one of these spacings. The models of Allen and Kollman⁸ and Lippincott *et al.*² are compatible with a spacing of $0.42\ \text{nm}$, if an $\text{O} \cdots \text{O}$ distance of $0.24\ \text{nm}$ is assumed.

X-ray diffraction has shown that the calcium fluoride used previously to produce "fluorite polywater"¹ was cleaved along the 531 crystal plane. The spacing of fluorine atoms in this plane is $0.386\ \text{nm}$ ¹⁴, therefore any model similarly proposed to explain the infrared spectrum of fluorite polywater must fit this spacing.

We feel that these experimental distances provide a more rigid criterion for models of polywater than those used previously, and conclude that most present molecular models must be considerably modified, if not entirely discarded, as a result of the evidence presented here.

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Ball Lightning and After-images

ARGYLE¹, in writing from a distinguished observatory, suggests that observations of ball lightning are optical illusions, and also claims that he has "found it easy to simulate with light bulbs" a phenomenon which he has apparently never witnessed and the reports of which he is not prepared to accept.

No one will deny the existence of after-images and most people have experienced them on several occasions, but after-images which appear to more than one differently sited observer to have precisely the same form and to travel the same path; which clearly emerge from doorways, are occulted by nearby objects, yet obscure those just behind; which have angular diameters increasing from five or six degrees to over twenty degrees as they pass from over two metres to within fifty cm of the observer², require remarkable properties of the retina or extraordinary hallucinations on the part of the observer.

When I recorded an observation of ball lightning² I did not mention that my account tallied precisely with that of the only other occupant of the passenger cabin, a terrified air hostess who was strapped in her seat on the opposite side and farther to the rear of the aircraft. She saw the ball continue to travel down the aisle and finally disappear towards the lavatory at the end. I had no alcohol on this flight.

A very similar account of ball lightning in an aircraft is quoted by Uman³. The ball in this case was larger and of a different colour, possibly as a result of different pressure and slight contamination of the air in the cabin of the aircraft.

Ashby and Whitehead⁴ suggest that ball lightning appears around negatively charged cosmic dust particles of antimatter which descend to ground level. They offer no explanation of the usual suspension of these balls within a few feet of an earthed surface or how the antimatter dust enters an aircraft cabin where it is transformed into a glowing and unerringly moving ball. They do not account for the typical speed of motion or for the shape and size, unless they intended to imply that the size of the ball and its brightness distribution are governed by the mean free path of the ionizing decay fragments. A further problem with this process is that the measurements of cosmic dust in space do not, as yet, indicate that any of the particles are from beyond the solar system, although particles of less than 1 μm diameter with hyperbolic velocities, such as one claimed by Otto Berg⁵, could be expelled by radiation pressure on the fragmentation of larger particles near perihelion⁶. The implication of Ashby and Whitehead's note is therefore that the solar system is well endowed with larger bodies consisting entirely of antimatter.

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After-images and Ball Lightning

ARGYLE¹ has revived suggestions²⁻⁴ that descriptions of ball lightning may simply represent some form of optical illusion. In particular, he postulates that the "bright spheres" are positive after-images caused by observation of short lived effects from nearby lightning strokes. On this view, the apparent movement of a "sphere" is due to the projection of the fixed retinal after-image against different backgrounds, as a result of voluntary or involuntary eye movements.

An obvious difficulty is to account in this way for reports of noise or smell accompanying the disappearance of ball lightning and for occasions when several observers are involved^{5,6}. Argyle suggests that it may be possible to ascribe these and other effects to the peculiar psychological state of people who have narrowly escaped being struck by lightning, and to dismiss those reports where the ball causes damage as "unreliable". But after-images do not remain more or less constant in colour like most lightning balls may change in colour in ways that depend on the initial adaptation of the observer, the primary stimulus and the secondary stimulus or background against which the after-image is viewed⁷. Moreover, an after-image which has disappeared may be recovered by blinking, a change in luminance of the background or by eye movements—an effect not yet reported for ball lightning.

The chief difficulty in the after-image hypothesis is, however, in the reported size of most lightning balls, which are usually said to have a diameter in the range 10–20 cm and to remain constant in size whatever the path followed by a ball^{5,8}. After-images appear to be localized at or in front of the background against which they are viewed, which implies that if the background recedes, the after-image also appears to recede and the observer believes that it has increased in size^{7,9}. On the after-image hypothesis, then, it would be expected that a common feature of all reports would be a direct relationship between apparent diameter and estimated distance. Such a relationship is conspicuously absent in reports of ball lightning.

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Ball Lightning or Spots before the Eyes?

WITH continuing unsatisfactory attempts to give ball lightning a convincing physical basis, it is no surprise that its objective reality has at last been called into question by Argyle¹. Once again physical scientists are asked to adopt the philosophy that if a phenomenon is difficult to explain physically then it cannot be real.

Argyle attempts to explain ball lightning in terms of positive after-images, which have certain properties in common with the former. There seem to be two overriding objections to this conjecture. First, it is hard to understand the unanimity of description in cases where there have been many witnesses, if the explanation is physiological and psychological. The probability that all the passengers of an aircraft will simultaneously experience corresponding positive after-images (which Argyle admits is a rare occurrence) must be very small indeed. Second, with so many more ubiquitous sources of bright lights other than lightning in the environment (the Sun, artificial lights against a dark background and so on) it is hard to understand the association with thunderstorms. Of course, all this presupposes that we ignore the cases involving direct physical effects, which Argyle suggests.

This appeal to physiology, then psychology, to explain embarrassing puzzles in physics epitomizes a quite general and interesting tendency in the scientific community. We are presented with two varieties of phenomena in science, which we may loosely call "laboratory" and "natural". The first variety is reproducible and can be subjected to experimental manipulation, or is at least predictable in advance. The second variety is unreproducible and unpredictable (consisting of, for example, meteorites, ball lightning, novae) and if also transient the experimenter is fortunate indeed to have his apparatus at the right place at the right time. Consequently, science must rely for its information on that much mistrusted individual, the layman, to whom is attributed the property of being able to observe objectively anything that can be explained, but imagining everything that can't. History is replete with examples, not least that of the meteorite. Necessarily, a subjective explanation loses its credibility if one is presented with tangible physical evidence, such as the barrel of water incident². In this case the usual procedure is to deny the veracity of such reports. The philosophy of this approach seems to be that if a naturally occurring phenomenon is hard to account for conventionally (i) decide that it has no physical reality; (ii) construct a physiological or psychological explanation; (iii) ignore the physical evidence that contradicts this explanation.

All this bears a striking resemblance to the mistreatment of that other perennial and highly disreputable subject of unidentified flying objects, to which the above philosophy has been consistently applied for 25 yr. The final irony is that a section of the Condon report on unidentified flying objects is devoted to an explanation of these phenomena in terms of ball lightning, by Altschuler³.

Incidentally, in the same section he mentions the possibility of the formation of luminous balls by micrometeorites of antimatter entering the atmosphere, which was discussed by Ashby and Whitehead⁴, and to which they do not refer.

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Received March 29, 1971.

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BIOLOGICAL SCIENCES

Brachiation and the Early Evolution of the Hominoidea

A ONCE popular view among anthropologists was that many of the morphological features common to man and the living apes (especially the gorilla and chimpanzee) could be attributed to a shared evolutionary phase of brachiating locomotion. It was further plausibly suggested that such arboreal suspensory activity could have provided an excellent apprenticeship for the adoption of erect bipedal posture by the early terrestrial hominids.

In the past decade fashion has tended to favour the alternative notion that man is only distantly related to the living apes, and that the Hominidae and extant Pongidae were independently derived from those early or middle Miocene dryopithecines which have been dubbed "dental apes"—primates which supposedly combined a hominoid dentition with limbs which retained a more primitive quadrupedal monkey-like morphology. The discovery of the almost complete forelimb bones of *Dryopithecus* (*Proconsul*) *africanus* and their description by Napier and Davis¹ have provided the keystone of this hypo-

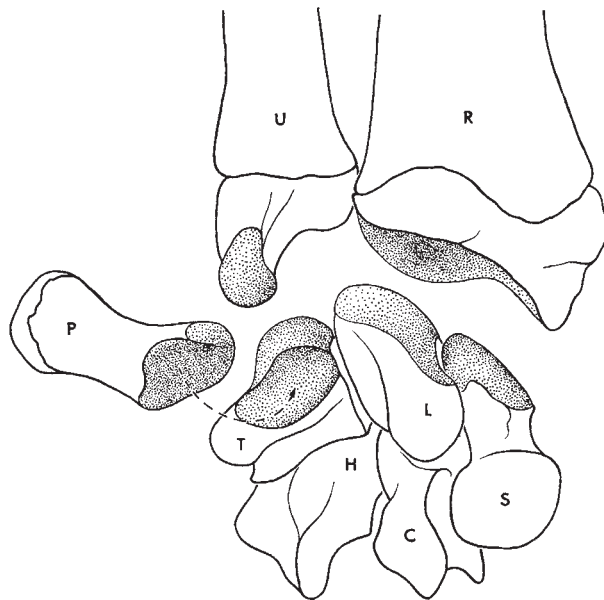


Fig. 1 The palmar aspects of the bones entering into the left wrist joint (with the articular surfaces participating in this joint stippled in each case), together with the capitate and hamate, in *Procolobus verus*. R, Radius; U, ulna; S, scaphoid; L, lunate; T, triquetrum; C, capitate; H, hamate; P, pisiform (rolled away from its articulation with the remainder of the carpus).

thesis. Such a forelimb, said to preserve an essentially quadrupedal type of wrist articulation, but showing incipient brachiating features in other parts, has been suggested as a reasonable prototype for that of terrestrial hominids on the one hand, and pongids, with an arboreal brachiating ancestry, on the other. Implicit in this popular view is the belief that many of the anatomical similarities between the two families are the result of parallel evolution.

Recent studies²⁻⁴, however, have shown that all living hominoids, including man, possess a unique structural modification at the wrist, involving the emergence of an evolutionary novelty—an intra-articular meniscus—which to a varying degree excludes the ulna from articulation with the carpus. There are ample grounds for assuming that the appearance of this structural modification was functionally correlated with a capacity for brachiation, a locomotor method which demands an increased range of supination as the body swings forwards suspended from one hand, rotating about this grasp towards a grip with the other hand; such rotation is achieved by supination of the grasping limb. This improvement in a key morphological component, the wrist joint, might then have provided the basis for a new repertoire of versatile suspensory locomotor and feeding behaviour, of which brachiation is one manifestation. As this unique forelimb morphology is clearly part of the heritage of all living hominoids, the status of the Miocene dryopithecines as possible candidates for the source of the diverging hominid and pongid lines needs review; it is most unlikely that the stem form could have possessed the wrist structure of an arboreal quadruped.

The elaboration of the hominoid meniscus involves considerable remodelling of the ulnar side of the wrist; the imprint of these structural changes is apparent even on the dry bones. A detailed account of these osteological features and their functional significance will be published later, but Figs. 1 and 2 illustrate some of the contrasting structural features in the bones of the monkey and ape wrist. In monkeys (*Cercopithecoidea* or *Ceboidea*), the ulnar styloid process articulates with both triquetrum and pisiform; it functions in a way similar to that of the lateral malleolus of the hind limb and accordingly its articular surface faces the interior of the joint. The weight-bearing triquetrum is a relatively large block-like bone firmly

sited on the hamate which lies rather obliquely, in such a way that it often virtually excludes the capitate from articulation with the lunate. The pisiform completes the weight-bearing cup on the triquetral by articulating at its palmar margin, projecting proximally to form the bony element of the "heel" of the hand. In the chimpanzee the articular facet on the ulnar styloid process (for the meniscus in this case) is now peripheral. The reduced triquetral (here appropriately named), the convex summit of which articulates with the meniscus, lies on the ulnar margin of the carpus, borne on a spiral facet (similar to that of man) on the vertically aligned hamate which retains only a limited contact with the lunate. The pisiform projects distally into the palm, this changed inclination entailing a major remodelling of its articular surfaces for the triquetral and the periphery of the meniscus. Examination of the casts of the relevant forelimb bones of *Dryopithecus (Proconsul) africanus* (Fig. 3), held in the British Museum (Natural History), leaves little doubt that they were associated in a quite advanced type of meniscus-containing wrist joint.

There thus seems to be a reasonable basis for the belief that anatomical changes at the wrist favouring suspensory forelimb locomotion were already well established in the early Miocene Hominoidea and presumably played an important, and perhaps decisive, part in the early emergence of the superfamily. It is well recognized by palaeontologists that the rapid evolution of a key character complex may lead to the emergence of new higher taxonomic categories; a commonly cited example is that of the tarsal joint changes which apparently led to the emergence of the order Artiodactyla⁵.

It is interesting to note that gibbons, although possessing a prominent meniscus (containing a bony lunula) at the wrist, present a carpus less modified in its osteological features even than that of *Dryopithecus (Proconsul) africanus*: the form of the hylobatid pisiform and triquetral is more reminiscent of that of monkeys than of apes. This suggests a very early separation of the gibbons from the emergent Hominoidea and is in keeping with the current trend to accord them separate familial status (Hylobatidae). The closer relationship of man to the African great apes, and to their presumptive early (or middle) Miocene ancestors, follows logically. This view of the historical affinity between man and *Pan* and *Gorilla* accords well with the modern biochemical findings of evolution at the

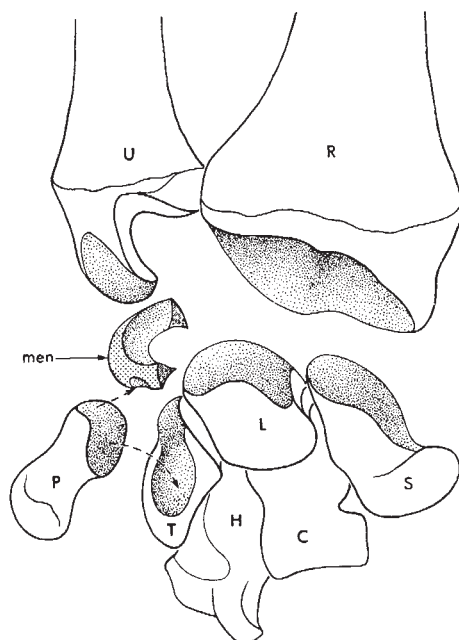


Fig. 2 The left wrist of *Pan troglodytes* showing the region comparable with that illustrated in Fig. 1, similarly labelled. Part of the meniscus (men) is shown, its horns of attachment to radius and lunate having been removed.

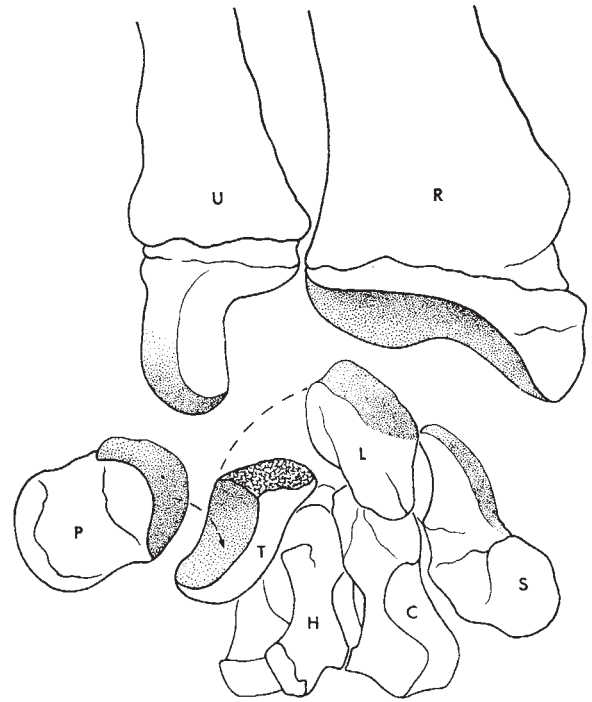


Fig. 3 The left wrist of *Dryopithecus (Proconsul) africanus* showing the region comparable with that illustrated in Figs. 1 and 2. The missing portion of the triquetral is indicated by a broken line.

molecular level^{6,7}. Consideration of structural modifications at the wrist joint makes it probable that the hominid line diverged when these adaptations, presumptively correlated with suspensory locomotion, were at a somewhat more advanced stage than in *Dryopithecus (Proconsul) africanus*. This would not necessarily conflict with the view of Simons and Pilbeam⁸ that *Ramapithecus punjabicus*, of the late Miocene or perhaps early Pliocene, was an early hominid. It would seem unlikely, however, that hominid origins could have been as recent as 3.5–5 million years ago, as suggested by Sarich⁷, using the evolution of the albumin molecule as a biological clock. In spite of the lack of precise indications as to the time of origin of the hominid line, there now seem to be adequate morphological grounds for a return to the view that man and the African great apes share a history of specialized suspensory arboreal locomotion. The indications are clear that the ancestral middle Miocene hominoids were structurally and functionally advanced in this locomotor style; the currently popular view that they were comparable in limb structure to living semi-brachiating monkeys is no longer tenable. The anatomical changes briefly noted here, bringing with them the enhanced mobility of hand on forearm so essential during suspensory locomotion, must have played an important part in the emergence of man, for they are also clearly preadaptive to efficient use of the hands as manipulative organs, in such activities as food gathering and transport, and tool use and tool manufacture.

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Self Righting by Tridacnid Clams

TRIDACNID clams can be divided into two distinct groups on the basis of whether they are physically fastened to the substrate. Of the six species comprising the family Tridacnidae¹, *Tridacna crocea*, *T. maxima* and *T. squamosa* live byssally attached to dead coral, coral rubble or limestone during the whole of their adult lives. The other species, *T. gigas*, *T. derasa* and *Hippopus hippopus*, live byssally anchored as juveniles, but when approaching maturity their byssus glands atrophy, and the adult clams take up unattached existence on coral rubble or hard packed sand. This habitat difference is also expressed in the weight and morphology of their shells. The byssally attached species possess shell valves which are in most respects larger editions of those found in other bivalves (Fig. 1A). The unattached clams, on the other hand, possess bizarre shells which are unusually massive resulting from a unique deposition of solid shell material within the cavities of the umbones (Fig. 1B).

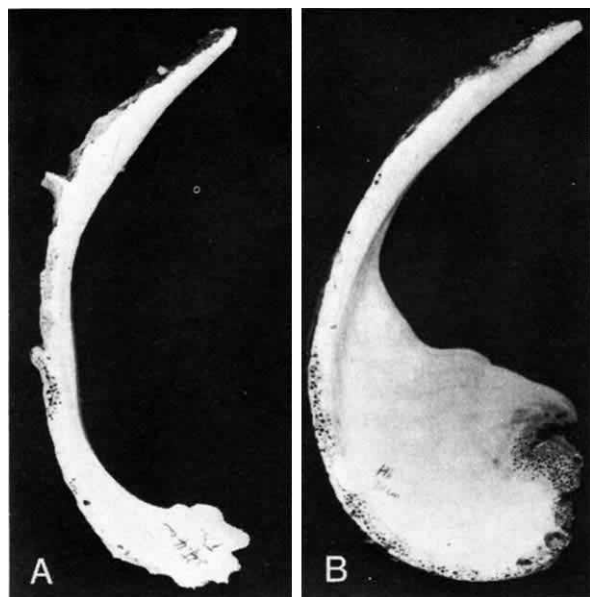


Fig. 1 Diamond saw cut cross sections through the umbones of two tridacnids. A, *Tridacna squamosa*, a byssally attached clam (length 24.4 cm). B, *Hippopus hippopus*, an unattached species (clam length 34.0 cm).

When unattached tridacnids rest their umbones and hinge lines on the substratum the symbiotic zooxanthellae contained in their hypertrophied siphonal tissues^{2,3} are exposed to the Sun. Extensive thickening of the umbones increases the clam's postural stability by adding to its mass and also lowering its centre of gravity. This increase in resistance to movement by the shell insures that the usual posture will not be upset in normal surf and current conditions. During storm conditions, however, some clams are toppled by increased wave force, and smaller individuals may roll for a short distance across the reef flat. Larger clams, however, are rarely observed *in situ* which are not in the upright condition. Are the clams immediately self righting because of their low centre of gravity

or, once toppled, do they go through a righting response in order to regain their original position?

Purchon⁴ favours the former hypothesis. He describes how *Hippopus hippopus*, which he mistakenly claims to be the sole free-living tridacnid, is rolled about by the surf during certain stages of the tide. He suggests that the heavy deposits of nacre within the umbone cavities provide the clam with an "automatic righting system". Thus, no matter how much the shell is rocked by the waves, the shell always comes to rest with the umbones in the lowest position. My observations on unattached tridacnids, made during two 1 month periods in the field at Eniwetok Atoll, Marshall Islands, failed to substantiate those of Purchon. The morphology of the shell valves suggests that the clams might perform as Purchon has observed, but, in fact, the living clam in its reef habitat may be rolled on its side, on end, or upside down without automatically righting itself. Instead, toppled adult specimens of both *Hippopus hippopus* and *Tridacna gigas* go through the step-wise sequence illustrated for *H. hippopus* in Fig. 2A-C and so right themselves.

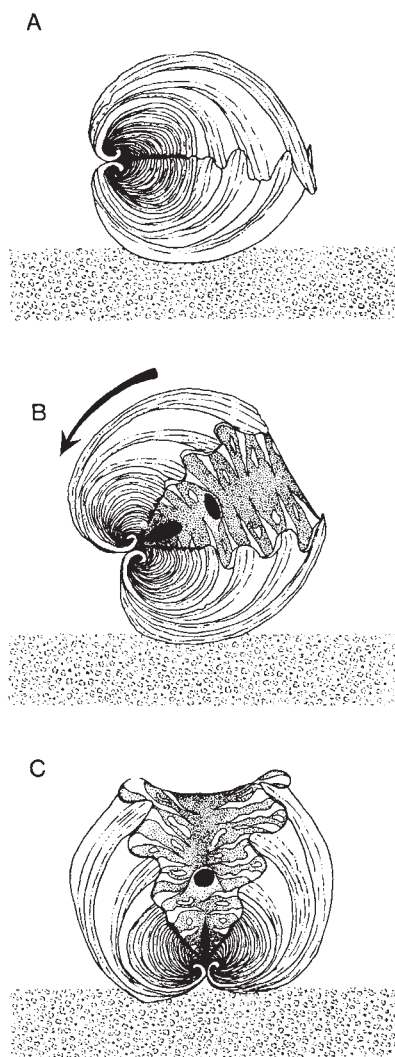


Fig. 2 A-C, The step-wise sequence of self righting by an adult *Hippopus hippopus*.

In Fig. 2A, the clam has just been placed on its side and, in response to both tactile and photic disturbance (a shadow cast on the exposed tissues), has tightly closed its valves. After some time (1-72 h), the clam's single adductor muscle completely relaxes and the elasticity of the hinge ligament

springs the clam's valves widely apart (Fig. 2B). As the valves spread apart, the uppermost umbone is displaced to one side, which unbalances the clam and causes it to roll over to its normal upright position (Fig. 2C).

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Nocturnal Songbird Migration

WE would like to comment on Evans's criticisms¹ of our recent article² concerning the influence of wind on the direction of nocturnal songbird migration. We pointed out that problems in identifying bird types from radar echoes may have contributed to the controversy about passerine nocturnal migrants compensating for wind drift. Evans claims that there is no difficulty in distinguishing between radar echoes from small land birds and those from waders and waterfowl in England. But his own radar work in Northumberland clearly demonstrates that this is not the case. In 1963 he attributed radar echoes of migrants in October and November to songbirds (wheatears, icelandic redwings, robins and song thrushes) and used these data to support his hypothesis that birds fly on fixed tracks, thus correcting completely for the drifting effects of the wind³. In a later article⁴, there is the following statement (pages 54-55): "However, records from October and November are excluded from this paper, because echoes from waders are difficult to distinguish from those from larger passerines, for example migrant thrushes, whose movements often overlap in timing, area of departure and direction with those of waders".

Evans implies that we selected the data in our article to support the hypothesis that passerine nocturnal migrants selectively fly downwind. We selected the nights to represent a broad spectrum of wind directions during each season. As Table 1 in our article shows, all four quarters of the compass are represented in each season. Our report was a preliminary analysis, but the data therein are representative of more than 300 nights of similar data we have collected to date.

We were remiss in failing to specify where the observations were made in the two seasons. The autumn data were collected at Lake Charles, Louisiana; the spring data at Athens, Georgia. Thus, Evans's comments concerning the wind shift in spring do not apply. The birds involved in the migrations, before and after the wind shifts, may have belonged to different populations. They were, nevertheless, flying downward in the air mass in which they were migrating, and the change in migration direction often occurred rapidly (within half an hour, or less) when the wind shift was abrupt.

Evans is correct in that our data cannot resolve the question of whether birds fly on chosen tracks or chosen headings. In downwind flight, track and heading are the same, and the question of drift by wind, or correction for drift, does not arise. This was precisely the point of our article; that is, that many passerine nocturnal migrants selectively fly downwind, regardless of the direction of the wind. We have since shown⁵ that

waders and waterfowl probably use a different method of flight orientation because they frequently correct for drift in winds of moderate speed.

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First Record in Scotland of the Leopard-spotted Goby, *Thorogobius ephippiatus*

THE leopard-spotted goby was first discovered by G. R. Forster of the Plymouth laboratory of the Marine Biological Association in 1955, and was described as a new species, *Gobius forsteri*, by Corbin¹. It is interesting that the original record was made while aqualung diving, and that subsequent evidence of the occurrence of the fish around British coasts has continued to be provided largely by divers' sightings and photographs. The apparent restriction of this locally common fish to crevices in rocky sublittoral areas had evidently prevented its discovery by conventional means of collection such as dredges and trawls, which are notoriously inefficient at sampling this type of substrate.

G. forsteri has subsequently been identified with *G. ephippiatus*, Lowe 1839, by Miller², who proposed the inclusion of the species in a new genus, *Thorogobius*. Miller described the distribution of the fish as warm temperate Atlantic-Mediterranean, extending as far north as the Isle of Man and the north coast of Ireland. By analogy with related gobies of similar distribution, he forecast the occurrence of *T. ephippiatus* along the west coast of Scotland, or even as far as the south-west coast of Norway.

The prediction for Scotland has now been confirmed by the sighting of a single specimen (Fig. 1) which extends the known range by more than 350 miles. It was discovered on August 15 during a dive 1 mile south of Wick, Caithness. In this area the Caithness flagstone series of the Old Red Sandstone is almost level bedded and, by differential weathering both above and below sea level, these sandstones are eroded into deep horizontal ledges which provide an ideal habitat for the



Fig. 1 The leopard-spotted goby, *Thorogobius ephippiatus*, recorded off Caithness, Scotland.

species. The specimen was found at a depth of 10 m in just such a crevice, in an otherwise vertical rock slab.

Comparison of surface sea temperatures shows that the mean annual temperature in this region is 9.1° C, as against 10.2° C in northern Ireland. The winter minimum temperatures off Wick are similar, however, to those in the Irish Sea where *T. ephippiatus* is known to occur. Closer examination should reveal the presence of the leopard-spotted goby along the Scottish west coast where mean annual and winter minimum temperatures are higher than those in the north-east corner of Scotland. Because of the small size and secretive habits of the fish this sighting should be considered as a real extension to the known range of the species, as opposed to the records of warm water pelagic fish which are more subject to accidents of water currents and drift.

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Calcium Shift into Bone causing Transient Hypocalcaemia after Injection of Parathyroid Hormone

AFTER intravenous injection of parathyroid hormone (PTH) in man and several animals, the plasma calcium concentration decreases transiently before rising, and this effect is usually attributed to calcitonin contamination of the parathyroid hormone. We now report an investigation in the rat with calcitonin-free hormone which shows that the transient hypocalcaemia is due to PTH itself and results from a rapid flow of calcium into the skeleton. These results supply evidence to strengthen current suggestions that entry of calcium into bone cells occurs very early in the response of PTH and may represent its primary action.

The study was undertaken as part of an investigation of the rapid response to PTH previously reported in isolated blood-perfused bone¹. Results of injecting low doses of PTH (20 USP units/kg) intravenously to dogs have been described before². They too show a small but consistent fall in plasma calcium concentration. In that animal the greatest lowering was reached 20 min after injection and averaged 4% of the resting level.

A preliminary experiment showed that in rats, as in dogs, intravenous injection of PTH initially lowered the plasma calcium concentration. The effect was absent in a group of animals which received a corresponding weight of PTH inactivated by oxidation of the methionine⁸. The lowering was greatest between 5 and 10 min and by 20 min the calcium had returned to its resting level. Results of the subsequent study are given in Table 1, which shows that at 10 min the mean calcium fall was 3%. This effect was significant. The concentrations of magnesium and phosphate in the same samples were not significantly changed, although the phosphaturic action of PTH is known to begin within 1 min⁹.

In the dog study reported elsewhere² it was concluded that the hypocalcaemia was due to calcium flow out of the blood. This study supports this conclusion and shows that the principal site of calcium uptake is the skeleton. The fraction of the isotope dose taken up was increased by PTH in all five samples of bone and decreased in all the soft tissues examined (Fig. 1). Less than 0.1% of the isotope dose found its way into the urine in this 10 min experiment and the proportion was even smaller in the PTH-treated rats, although the difference was not signifi-

cant. Less than 0.01% of the dose entered red cells. The fall in plasma radioactivity was highly significant ($P \approx 0.001$) and represents a 15% decrease, much larger than the 3% decrease in total calcium.

The total amount of calcium entering the skeleton in response to the PTH injection can be calculated from the change in calcium concentration of the plasma and ECF, and also by relating the specific activity of plasma calcium to the increase in skeletal uptake of radioactivity. Both calculations, which will be published in detail elsewhere, suggest that the net PTH-induced calcium entry was of the order of 50 µg.

There have been previous reports that extracts of parathyroid tissue have an initial hypocalcaemic effect when injected intravenously. Copp and Cameron¹⁰ observed the effect in anaesthetized dogs injected with commercial parathyroid extract (Lilly) and attributed it to the presence in this extract of the recently discovered hypocalcaemic hormone, calcitonin^{11,12}. Other authors noticed the initial calcium fall in injecting bovine parathyroid preparations in man¹³ and sheep^{14,15} and with partially purified human PTH in dogs¹⁶. None of the hormone extracts, however, was homogeneous and the calcium fall was generally attributed to calcitonin. Mulryan *et al.*¹⁷ previously studied the effect of parathyroid extract (PTE) on the distribution of radiocalcium in the rat, but injected the isotope 1 h after the hormone. They commented that if PTE exerted any influence on the transport of calcium into or out of cells it would not have been possible to demonstrate the effect with this timing of injections.

Our experiments, in which hormone and isotope were injected simultaneously, and the dog study² show that PTH itself causes initial hypocalcaemia when injected intravenously. This is probably due to a transient increase in calcium permeability of cell membranes, allowing a flux in the direction

Table 1 Results of Analysis of Plasma from Control and PTH-treated Rats bled 10 min after Intravenous Injection

	Calcium (mEq/l.)	Magnesium (mEq/l.)	Phosphate (mgP/100 ml.)
Control	4.26 ± 0.04	1.46 ± 0.04	7.59 ± 0.21
PTH-treated	4.13 ± 0.04	1.46 ± 0.04	7.66 ± 0.25
Significant change (%)	-3.0% ($P \approx 0.01$)	None ($P > 0.5$)	None ($P > 0.4$)

Means and standard errors from two groups of nine animals. Experimental procedure was as follows. The urethrae of male Wistar rats (95 g ± 4 g s.e.), starved overnight, were ligated under local anaesthesia. Sixty minutes later 0.3 ml. of test or control solution was injected via the tail vein, rats being taken at random and the treatments alternated. The control solution contained ⁴⁷CaCl₂ (2.5 µCi per rat) in the vehicle described elsewhere². The test solution was identical except for the addition of bovine PTH to give 30 USP units per rat. This submaximal dose would restore a normal plasma calcium concentration in parathyroid-ectomized rats of this size in the Munson PTH assay³. The PTH was purified to the stage of gel filtration on 'Sephadex' (1,500 U/mg) and radioimmunoassay showed it to contain no detectable bovine calcitonin (less than 10⁻¹⁰ g per rat dose). Animals were exsanguinated under halothane anaesthesia by cardiac puncture with open chest at 10 min (± 20 s) after injection. The first 2 ml. of blood withdrawn was transferred to a heparinized tube for analysis. Femora, scapulae and the tail were dissected and cleaned. Skin and muscle samples were dissected from the abdominal wall and the organs listed in Fig. 1 removed intact. Bladder contents plus saline washings were made up to 5 ml. with dilute hydrochloric acid. After weighing, all tissue samples were counted on a gamma spectrometer, together with 1 ml. aliquots of washed red cells, 2 ml. aliquots of the diluted urine, 0.4 ml. aliquots of plasma diluted to 2 ml., and appropriate standards. Results were corrected for radioactive decay and expressed as percentage of the dose. Plasma samples were analysed for calcium and phosphate by the combined atomic absorption method of Parsons *et al.*⁴ and for magnesium by the method of MacIntyre⁵. In calculating the proportion of the total dose of ⁴⁷Ca attributable to various tissues, it was assumed that in the rats used the muscle mass was 33% of the body weight⁶ and the plasma volume 3.1 ml. per 100 g body weight⁷. An average of 14 g for the whole pelt was determined by dissection and weighing.

of low-calcium intracellular fluid. Such an effect of PTH was demonstrated in Hela cells by Borle^{18,19}. Nagata and Rasmussen have inferred it in kidney tubules (cited in ref. 25) but ours is the first evidence for its occurrence in bone. We think the PTH hypocalcaemia develops faster than the early response to calcitonin, but direct comparison between the two is clearly required. Investigation of antagonism or reinforcement between them may cast further light on the mechanisms involved.

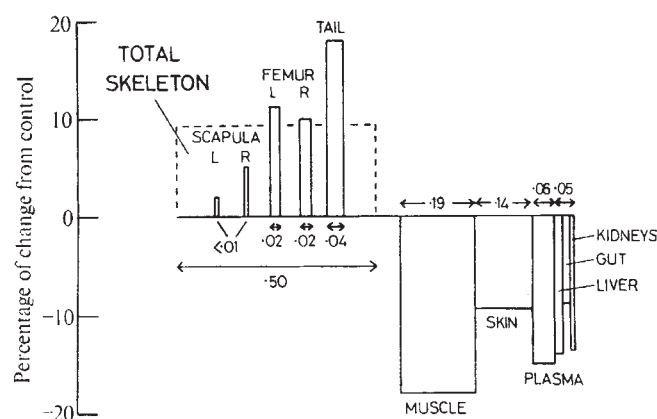


Fig. 1 Distribution of a dose of radiocalcium 10 min after intravenous injection, and the changes produced by adding PTH (30 USP units per rat) to the isotope solution. By making reasonable assumptions more than 90% of the dose was accounted for. Calculations are based on mean values, control and hormone-treated groups each containing nine rats. The width of each column (shown thus $\leftarrow 0.19 \rightarrow$) represents the fraction of the dose attributable in control animals to the tissues analysed. Where only a sample of tissue was taken, these dose fractions were calculated using the figures for total tissue mass given in the methods section. The figure for skin refers to the whole pelt. The height of each column represents the percentage change of tissue uptake in PTH-treated rats compared with controls. Assuming that in the controls half the dose of isotope had entered the skeleton at the time of sampling (see text), the dotted line approximately indicates the mean increase in skeletal uptake caused by the hormone. All differences between control and PTH-treated groups were significant ($0.001 < P < 0.01$) except those for the scapulae, which were particularly difficult to dissect without loss.

The proportionately greater effect of PTH on ^{47}Ca than on total calcium is probably a consequence of a compensatory flow of calcium from exchangeable pools which limited the decrease in plasma concentration caused by the outflow to bone. At so short a time after injection the concentration of isotope in these pools would be much less than in plasma and the change in plasma concentration of ^{47}Ca would not have been thus restricted. This explanation does not preclude the possibility that part of the action of PTH in increasing the rate of disappearance of isotope from the blood was simply due to a rapid increase in bone blood flow. Charbon²⁰ provided evidence for just such an acute rise in blood flow to liver and kidney after injecting PTH. Existing methods^{21,22} for estimating total skeletal blood flow depend on assumptions about the initial clearance of bone-seeking isotopes and can clearly not be used to test such a possibility. But even if PTH does affect bone circulation, this could not explain its hypocalcaemic action.

We have not established that the skeleton is the only site at which PTH causes calcium influx into cells. If the calcium permeability of other cell membranes did not change, radiocalcium uptakes in all the soft tissues would have fallen in the same proportion as the reduction of plasma isotope concentration in PTH-treated rats. The decreases in muscle, liver and kidneys were close to that in plasma, but the falls in skin and gut were noticeably less (Fig. 1). The possibility cannot be excluded that a permeability increase occurred in skin and gut

and that its effects were masked by the greater flux into the skeleton.

The relevance of the calcium shift into bone to the mechanism of action of PTH rests on observations that many of the characteristic biochemical effects of the hormone on bone cells can be imitated, *in vitro*, by increasing the calcium concentration of the medium. The arguments for this mechanism have been discussed elsewhere²³⁻²⁵.

Redistribution of radio calcium is already well developed within 2 min of PTH injection. The rapidity of the ion shift is comparable to that of adenylyl cyclase activation^{26,27}, phosphaturia⁹ and vasodilation²², all of which begin within 1 min. Calcium inflow to bone therefore appears to be a primary event in initiating the action of parathyroid hormone, and may be physiologically related to the increase in intercellular cyclic AMP as proposed by Rasmussen²⁸.

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Mean Red Cell Age as a Determinant of Blood Oxygen Affinity

LOOSENING of the bond between haemoglobin and oxygen promotes the release of oxygen to the tissues and thus compensates for hypoxia. Such a decrease in blood oxygen affinity occurs in the principal types of hypoxia¹⁻¹², presumably because of an adaptive increase of red cell organic phosphates, especially 2,3-diphosphoglycerate¹³⁻¹⁷. In the natural ageing of normal human red cells, there are changes in the electrostatic interactions involving haemoglobin which bring about an increase of the affinity of haemoglobin for oxygen¹⁸. Glutamic oxaloacetic transaminase (GOT) is active only in younger red cells and is a better and more stable indicator of mean red cell age than reticulocyte counts^{19,20}. Using red cell GOT activity as such an indicator of age, we have investigated the relationship between mean red cell age and both red cell DPG and oxygen affinity.

We took samples of venous blood into heparin from eighteen normal human subjects; in four subjects sampling was repeated about 6 months later for twenty-two studies.

Some of each fresh blood sample was centrifuged; the red cells were washed three times with 0.9% NaCl and haemolysed (1:200 dilution) by the addition of salt-free water¹⁹. The haemolysate was assayed for red cell GOT activity at 25° C on a Beckman DU spectrophotometer at 366 nm, according to the method of Karmen *et al.*²¹, using prepared Boehringer Mannheim GOT reagents (GOT-UV system, catalogue number MO-A 15871 TMAB).

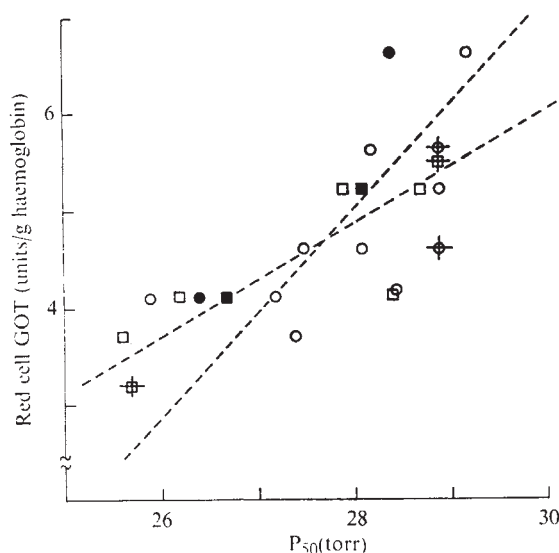


Fig. 1 Studies on blood of normal subjects. GOT, glutamic oxaloacetic transaminase. P_{50} , oxygen pressure at 50% saturation of haemoglobin at pH 7.40 and 37° C, without CO. $r = +0.733$; $P < 0.001$. Studies on women: unspecified, each studied once (○); specified, each studied twice (●, ⊕). Studies on men: unspecified, each studied once (□); specified, each studied twice (■, ⊕).

Red cell carbon monoxide (CO) was analysed spectrophotometrically in a 1:10 haemolysate by the method of Whitehead and Worthington²². We measured CO because it is increased in the blood of cigarette smokers, making some of the haemoglobin "inactive" (unavailable for binding oxygen) and increasing oxygen affinity of the remaining active haemoglobin²³. Standard haemoglobin, haematocrit, red cell and reticulocyte counts were also determined. Another portion of the blood was extracted in perchloric acid and analysed for DPG by method 2 of Towne *et al.*²⁴.

We determined oxygen-haemoglobin equilibria in the blood (containing 2.5 mg NaF/ml. blood) using the "mixing tech-

nique" at 37° C (ref. 25). The oxygen pressure (P_{O_2}) at 50% saturation of haemoglobin was corrected to a standard plasma pH of 7.40 from the measured pH using the nomogram of Severinghaus²⁶. We corrected to the CO-free state by adding 0.258 torr of P_{O_2} for every 1% saturation of haemoglobin with CO. With these corrections, the P_{O_2} of blood at 50% saturation of haemoglobin with oxygen is designated as P_{50} . The active haemoglobin, designated AHb, was calculated by subtracting CO-haemoglobin from total haemoglobin. The results were analysed by calculating the product-moment correlation coefficient (r) (ref. 27).

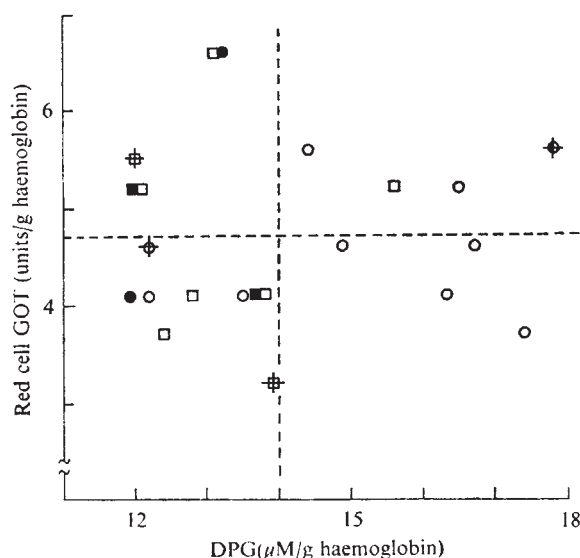


Fig. 2 Studies on blood of normal subjects. GOT, glutamic oxaloacetic transaminase; DPG, 2,3-diphosphoglycerate. Symbols as for Fig. 1. $r = 0$; $P < 0.9$.

Red cell GOT, a measure of mean red cell age, varied widely among individuals and for given individuals on different days about 6 months apart (Fig. 1). These observations suggest that erythropoietic activity fluctuates remarkably in normal individuals. Reticulocyte counts varied between 0.2 and 1.6%; there was no correlation between reticulocyte count and red cell GOT ($r = -0.288$, $P > 0.1$).

There was a highly significant positive correlation between red cell GOT and P_{50} ($P < 0.001$, Fig. 1). This confirms, by a different method, the previous observation of decreased haemoglobin-oxygen affinity (increased P_{50}) in young red cells compared with that in old red cells¹⁸. A relative increase in numbers of young red cells produces whole blood with a significantly decreased oxygen affinity. Because young and old red cells circulate together through the same vessels, this decreased oxygen affinity must be intrinsic, determined by the properties of young red cells, rather than being adaptive to extrinsic influences such as hypoxia or alkalosis.

In agreement with Hjelm²⁸, we found no correlation between red cell GOT and DPG ($P < 0.9$, Fig. 2). We seem to disagree with Bernstein²⁹ and Bunn *et al.*³⁰ who also used centrifugation and showed that young red cells contained increased DPG/g of haemoglobin. The reason for this disagreement is not clear. We also report DPG/g of haemoglobin. The same DPG measurements are sufficiently sensitive to confirm a previously reported negative correlation with AHb¹⁷ ($P < 0.01$, Fig. 3) whereas the corresponding P_{50} measurements do not correlate with AHb ($P > 0.1$, Fig. 4). We cannot exclude some change of red cell DPG with age. We consider any such possible DPG change an insufficient explanation of this large P_{50} change, suggesting that other influences play a role in regulating age-dependent haemoglobin oxygen affinity.

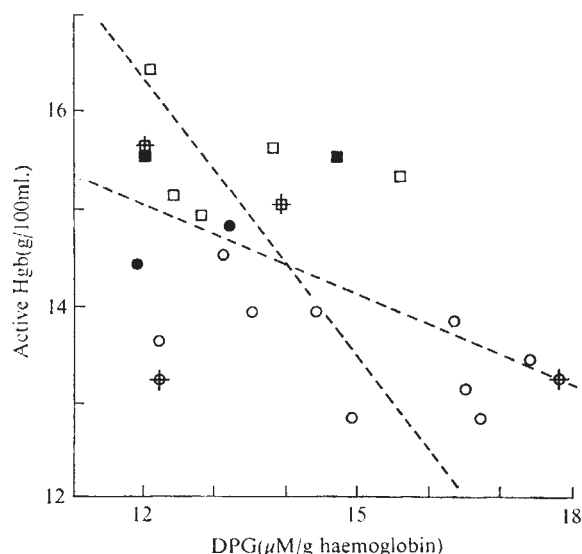


Fig. 3 Studies on blood of normal subjects. Active Hgb, total haemoglobin minus CO-haemoglobin. DPG, 2,3-diphosphoglycerate. Symbols are as for Fig. 1. $r = -0.574$; $P < 0.01$.

The correlation between DPG and P_{50} is not significant ($r = +0.156$, $P > 0.1$). In previous studies, acute hypoxia has been imposed causing increase of DPG and decrease of blood oxygen affinity¹⁶, but in our study all subjects are normal and unstressed. Within the normal range, the greatest variation of blood oxygen affinity is due to variation in mean red cell age which does not appear to require DPG.

In normal unstressed subjects, there is both variation of haemoglobin concentration affecting DPG which would ultimately influence blood oxygen affinity, and variation of mean red cell age affecting blood oxygen affinity through intrinsic mechanisms other than DPG. The oxygen affinity of blood in either health or disease must be the additive result of various extrinsic and intrinsic influences, not all mediated through DPG. A younger population of red cells would contribute to a useful decrease of blood oxygen affinity, either alone or supplementing that resulting from a hypoxia-generated increase of DPG.

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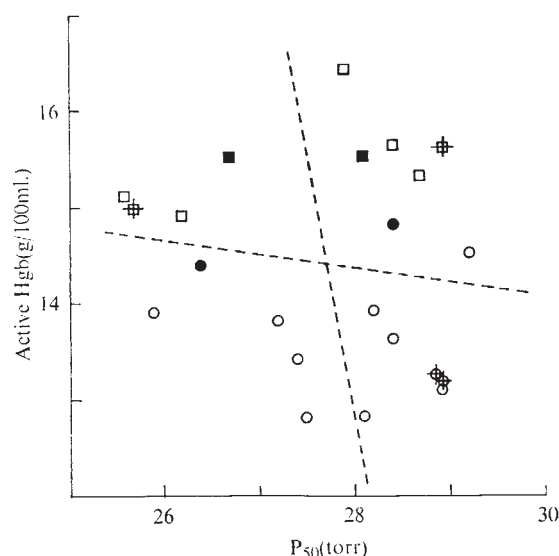


Fig. 4 Studies on blood of normal subjects. Active Hgb, total haemoglobin minus CO-haemoglobin; P_{50} , oxygen pressure at 50% saturation of haemoglobin at pH 7.40 and 37° C without CO. Symbols are as for Fig. 1. $r = -0.161$; $P > 0.1$.

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Monochloracetic Acids and Conodonts—a Warning

SINCE its introduction by Beckmann¹ in 1952, the monochloracetic acid method of processing limestones for conodont investigations has been the most widely used procedure in Germany and many other countries for the recovery of conodonts. Criticizing this method, Fahlbusch² stated that monochloracetic acid could etch or even completely destroy part of the conodont fauna, and implied that structural changes in conodonts might be caused by solution. Beckmann *et al.*³ were able to show by experiment and from experience that

Fahlbusch's contentions, based on erroneous theory and analogy, were not valid for the Devonian conodont faunas then under discussion. New evidence from the processing of Swedish Ordovician faunas indicates, however, that monochloroacetic acid can have a corrosive effect on some conodonts.

As part of a research project on cephalopod limestones, many samples of Lower to Middle Ordovician limestones from Sweden are being investigated, *inter alia*, for their conodont faunas. To recover the conodonts, the limestones are digested in monochloroacetic acid. We were surprised to find evidence of corrosion of conodonts in some of the Swedish Lower Ordovician epicontinental faunas. Such faunas should have been perfectly preserved according to Lindström, who digested his limestone samples in acetic acid^{4,5}. Additional material from the same samples was processed using monochloroacetic acid, but the conodonts in the residue were left in the acid for a shorter time in the second treatment. The difference in the recovery of the conodonts and in their preservation was so significant that we feel compelled to report our observations to colleagues working on, or about to work on, conodonts.

A rather striking example is one sample (Möckleby 13) of homogeneous Lower Ordovician limestone. In the first treatment 200 g of the limestone was left in the monochloroacetic acid for about 2 weeks. A scanty fauna of only six fragments of simple cone forms was recovered. The bases, apices, and margins were strongly corroded and the specimens barely recognizable to species. In the second treatment, another 200 g of the same limestone sample was digested in monochloroacetic acid, but every second day the acid was decanted, the residue recovered, and fresh acid was added. By this treatment the limestone yielded about 800 identifiable specimens. Most of these were well preserved, but some showed slight corrosion effects.

It is particularly significant that ramiform and prioniodiform elements can be dissolved if left in monochloroacetic acid for more than 2 days. The concentration of acid seems to be less critical than the duration of acid attack.

Clearly, selective corrosion by monochloroacetic acid might have affected the composition of conodont faunas recovered in the past. This may be the explanation of the relative scarcity of ramiform elements in Devonian faunas. But studies with the scanning electron microscope have shown that massive platform elements of the Devonian and Carboniferous have been virtually unaffected by monochloroacetic acid.

In this context, it is worth noting the use of formic acid to digest samples for conodonts. Formic acid dissolves argillaceous limestone faster and does so more effectively than either acetic acid or monochloroacetic acid. If they are left in formic acid for more than 1 day, however, conodonts can become corroded, or the microstructure can be so altered that the specimens collapse to a powder at the slightest touch.

Finally, we make the following recommendations. (1) The use of the monochloroacetic acid method of sample processing, which is fast and economical, should be continued for stratigraphical as well as other purposes, especially in routine work. (2) Residues should not be left in monochloroacetic acid for more than 2 days, regardless of the purpose of the study. (3) For research into the ultrastructure and micromorphology of conodonts, samples should be treated with acetic in preference to monochloroacetic acid whenever possible.

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Evidence for Presynaptic Dendrites and a Proposal for their Mechanism of Action

THERE is evidence that dendrites form presynaptic elements and that these synapses are involved in neuronal interaction in the amacrine cells of the retina¹⁻³ and the granule cells of the olfactory bulb^{4,5}. Recent evidence suggests that there are neurones which give rise to synapses from their dendritic branches in several areas of the central nervous system.

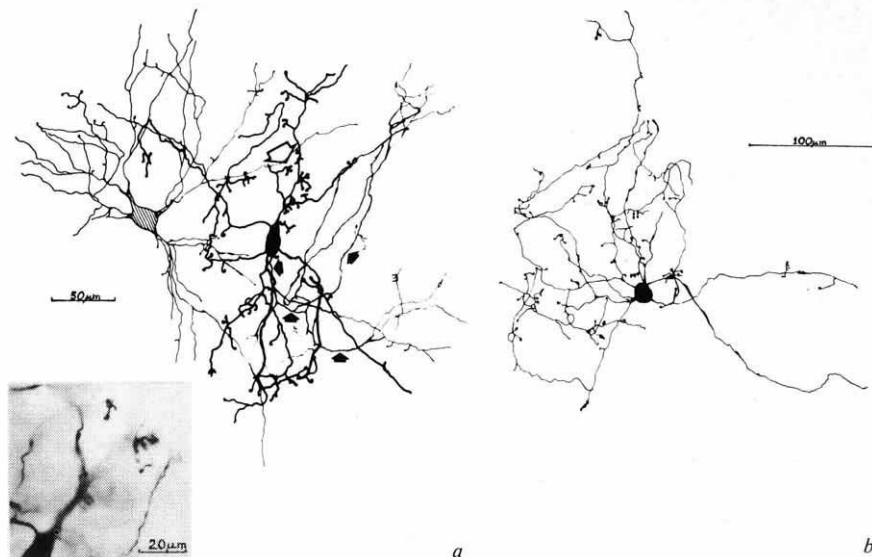
Profiles which seem to be dendritic⁶ but which also exhibit groups of synaptic vesicles have been illustrated in tissue obtained from the cat spinal cord^{7,8}, ventrobasal complex⁹, lateral geniculate nucleus¹⁰⁻¹², superior colliculus^{13,14} and medial geniculate nucleus¹⁵. The profiles identified as presynaptic dendrites lack the fine structural features of axonal initial segments¹⁶.

In Golgi-stained preparations of regions containing cells thought to give rise to synapses from dendritic processes, unusual cell types—for example, the amacrine cells of the retina¹⁷⁻¹⁹—are sometimes found which exhibit dendrites with numerous bulbous side branches. Some Golgi type II cells in the cat lateral geniculate nucleus have numerous fine or bulbous dendritic "spicules"²⁰⁻²². The most convincing correlation between an unusual cell type within the central nervous system and dendritic synapses has been presented by Lund¹³ in the superior colliculus of the rat. Lund found rather large Golgi stained neurones ("marginal cells") in the stratum zonale of the superior colliculus. Using the electron microscope he was able to identify similar cells and trace their dendrites from the cell body into the deeper layers of the colliculus where they gave rise to synapses.

This report is based on a study of the ventrobasal thalamus of two dozen adult cats, some of which were normal⁹, others surviving for various periods following ablation of the contralateral dorsal column nuclei²³, and a third group surviving for up to 6 months after large ipsilateral lesions of the somatosensory cortex. Normal adult thalamic tissue stained with the Golgi-Kopsch method²⁴ is characterized by large neurones (probably thalamo-cortical relay cells²⁵) with typical "tufted" dendritic branching patterns, and many smaller neurones with numerous fine dendritic appendages (Fig. 1). In some cases an axon may be seen to arise from the small cells and branch extensively in the region of the cell body (Fig. 1a). Other such cells have no demonstrable axon (Fig. 1b).

Electron microscopy of the cat ventrobasal thalamus reveals numerous apparently dendritic profiles which contain clusters of synaptic vesicles (Fig. 2a). These presynaptic dendrites contact either large or small dendritic profiles or cell bodies of large neurones of the nucleus⁹. Fig. 2a shows a structure interpreted as a dendrite: the synaptic vesicle accumulation within presynaptic dendrites of the ventrobasal thalamus is typical of that shown here; that is, the vesicles occupy less than half of the total area of the dendritic profile compared with profiles thought to be axon terminals in which the synaptic vesicles are distributed throughout the structure. Fig. 2b illustrates a small presynaptic dendrite and an adjacent profile with the characteristic features of axonal initial segments¹⁶. The difference in morphology between these two structures is apparent. Profiles interpreted as presynaptic dendrites have never been traced into axonal initial segments or myelinated axons. Fig. 2a is taken from an animal which survived for

Fig. 1 Projection drawings of cells from the adult cat ventrobasal thalamus stained by the Golgi method. *a*, The dendrites of the dark interneurone have numerous appendages some of which have bulbous tips. The axon of this cell is indicated by the dark arrows. The dendritic appendages at the open arrow are shown again in the photomicrograph at the lower left. A thalamo-cortico relay cell with "tufted" dendrites is lightly drawn in at the left. *b*, This cell has several fine dendrites which also exhibit numerous appendages. The cell did not reveal an axon.



30 days after a large lesion of the somatosensory cortex. It seems, therefore, that at least some of the dendritic synapses arise from cells which do not degenerate after removal of the somatosensory cortex. It is suggested that these are short axon cells (Golgi II neurones), such as seen in Fig. 1*a*.

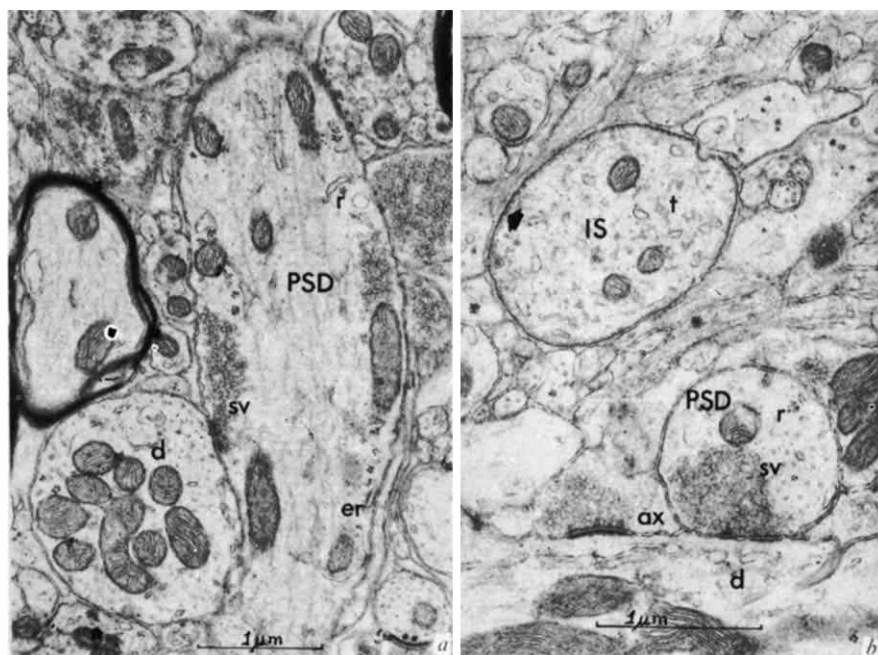
If the profiles identified in this study are those of presynaptic dendrites and these dendrites are derived from relatively small neurones within the ventrobasal complex, what could be the function of such cells? Golgi stains reveal that some have axons which arborize locally; these could influence other neurones within their field by means of a propagated axonal action potential. But the action potential may also invade the cell body and proximal dendritic tree of such cells (SD spike). Some of the proximal dendrites may give rise to synapses, and the action potential invading the soma and proximal dendrites may cause the release of synaptic transmitter from these dendrites. In some cells in the rat spinal cord²⁶, the frog optic tectum²⁷, and the lateral geniculate nucleus of the squirrel monkey¹¹, somatic synapses have been described, and the cell body itself may be capable of transmitter release.

It is unlikely that a spike in the region of the cell body is capable of invading the more distal dendritic branches which give rise to dendritic synapses, because of the rapid decrement

in the propagated impulse along branching dendrites²⁸. The finer dendritic branches are probably depolarized by synapses impinging upon them; a relatively large potential change would be expected because of their small diameter²⁹. It is not known whether this depolarization would result in a dendritic spike³⁰. It is possible that local dendritic depolarization without initiation of a propagated potential would be adequate to release transmitter. In a study of the giant synapse of the squid stellate ganglion, Kusano³¹ has shown that a 25 mV depolarization of the axon terminal is adequate to elicit transmitter release as demonstrated by a measured post-synaptic response. Kusano has suggested that transmitter release may be elicited by as little as a 10 mV presynaptic depolarization. Depolarization of fine dendritic branches may thus be adequate for transmitter release from these dendrites whether or not a propagated spike is produced.

Each of the separate branching elements of the dendritic tree of these cells might therefore be capable of releasing its transmitter regardless of the activity of other dendritic branches of the same neurone. In effect, this neurone then would have several independent spheres of influence represented by each of its arborizing dendritic branches. Each one of these dendritic branches could release transmitter. A schematic

Fig. 2 *a*, Electron micrograph of a presynaptic dendrite (PSD) of the ventrobasal thalamus 30 days after a large lesion of the ipsilateral somatosensory cortex. The dendrite contains granular endoplasmic reticulum (er), free ribosomes (r) and synaptic vesicles (sv). It forms a synapse with a dendrite (d). *b*, Normal cat ventrobasal thalamus. A presynaptic dendrite (PSD) containing ribosomes (r) and synaptic vesicles (sv), which contacts a dendrite (d). A profile containing fascicles of microtubules (t) and dense material (arrow) apposed to the inner layer of the plasma membrane is interpreted as an axonal initial segment (IS). ax, Axon terminal.



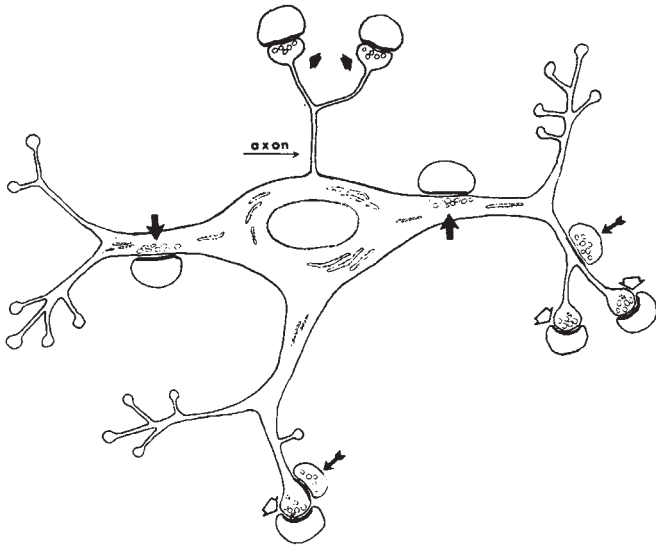


Fig. 3 A diagrammatic representation of the postulated mode of function of neurones possessing presynaptic dendrites. An action potential which is generated in the axonal initial segment would travel out along the axon and also invade the cell body and proximal dendrites. The axon terminals (small dark arrows) and proximal dendrites (large dark arrows) of this cell might all release synaptic transmitter more or less synchronously. However, the action potential would fail to invade the fine distal dendritic branches. The presynaptic dendrites of the distal branches would be depolarized by synaptic terminals contacting them (tailed arrows) and release their synaptic transmitter upon adjacent neuronal elements (open arrows), independent of the activity of other regions of the cell. Thus, each fine dendritic arbor might act as an independent synaptic unit.

representation of the proposed activity of the cell is shown in Fig. 3. An action potential arising in the vicinity of the cell body would propagate along the axon and into the proximal dendritic branches of the cell. The axon terminals and the proximal dendrites giving rise to synapses would release their transmitter at approximately the same time, allowing for different conduction rates. The action potential, however, would not succeed in invading the finer branches of the dendritic tree. These finer branches would be under the influence of synapses impinging directly upon them, and if adequate depolarization of the fine branches occurred they would then release transmitter on the postsynaptic elements which they contact. Each branch would thus independently influence postsynaptic elements.

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Effect of Lithium Ions on the Release of Acetylcholine from the Cerebral Cortex

THE addition of lithium ions to the fluid bathing *Aplysia* ganglion cells results in presynaptic electrical changes consistent with decreased acetylcholine (ACh) release¹. To ascertain directly the effect of lithium on ACh release from mammalian brain, Bowers and Rozitis² injected rats with lithium chloride and measured the release of endogenous ACh from electrically stimulated cortical brain slices, but did not find a significant difference in the electrically stimulated release of ACh in slices prepared from animals injected with sodium chloride compared with lithium chloride. They concluded, therefore, that lithium ions do not decrease ACh release in mammalian brain. But they allowed the possibility that certain more physiological forms of ACh release in the brain might be influenced by lithium.

We describe here how local replacement of sodium ions by lithium in Ringer-Locke solution affects spontaneous and evoked release of ACh from the cat cerebral cortex.

Experiments were performed on cats anaesthetized with a mixture of diallyl-barbituric acid and urethane (DIAL, Ciba, Ltd.) given intraperitoneally (0.6–0.7 ml/kg). ACh was collected from the exposed surface (0.72 cm²) of the pericruciate cortex, using the 'Perspex' chamber technique³. The chambers were filled with 1 ml. of Ringer-Locke solution containing eserine sulphate (1 × 10⁻⁴ g ml.⁻¹, British Drug Houses) and aerated with 5% carbon dioxide in oxygen. The Ringer-Locke solution had the following ionic composition: 137.0 mM NaCl; 2.5 mM KCl; 2.0 mM CaCl₂; 1.0 mM MgCl₂; 1.0 mM Na₃PO₄; 12.0 mM NaHCO₃; and 11.0 mM glucose. When sodium was replaced by lithium, sodium chloride was replaced by an equivalent molar amount of lithium chloride; the other ions, and the concentration of eserine, remained constant. ACh was sampled from the surface of the cerebral cortex unilaterally for fifteen periods of 15 min. The usual procedure was as follows: two resting samples alternated with a stimulated one, first with normal (137.0 mM NaCl) Ringer-Locke and then the sequence was repeated with sodium-free (137.0 mM LiCl₂) solution. In this way, we were able to

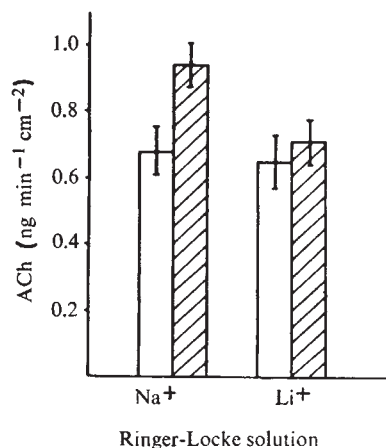


Fig. 1 The mean rate of acetylcholine release ($\text{ng min}^{-1} \text{cm}^{-2}$) from sensory-motor cortex into Ringer-Locke solution containing sodium and/or lithium ions. Each histogram is the mean ($\pm$ s.e.) of ten determinations. White columns depict unstimulated ACh release, and shaded columns stimulated ACh release.

detect a significant change in the release of ACh, which was reproducible. Immediately after removal, samples were frozen and stored at -18°C .

Blood pressure was measured in the right carotid artery within 6–12 h of collection⁴. Lithium Ringer-Locke solution had no obvious effect on the arterial blood pressure or on the shape of the dose-response curves to standard ACh solutions. The stimulating pulses were usually supramaximal rectangular pulses lasting 1 ms, delivered at a frequency of 1 s^{-1} to the contralateral forepaw, through a radio-frequency isolation unit of the Grass S8 stimulator. The efficiency of stimulation, and the influence of sodium ion replacement with lithium, were checked by recording the evoked potential with a cathode ray oscilloscope. The results were analysed statistically with Student's *t* test.

When the sodium chloride of the Ringer-Locke solution was replaced by lithium chloride, in each of ten experiments there was no significant change in the amount of ACh collected from the surface of the cerebral cortex, in the absence of peripheral stimulation (Fig. 1). Mitchell⁵ reported that electrical stimulation of a peripheral sensory nerve increased the rate at which ACh was liberated from the surface of the contralateral sensory cortex. Using this procedure we have found that with the solution containing lithium chloride, instead of sodium chloride, there is no increase in the output of ACh during peripheral stimulation (Fig. 1). This effect was readily reversed by restoring sodium ions to the collection fluid.

When peripheral sensory nerves were stimulated, transmission of afferent impulses, as indicated by the size of the response registered on the surface of the contralateral sensory cortex, was depressed. This depression occurred 10–15 min after the onset of superfusion of the cerebral cortex with lithium Ringer-Locke solution. Re-introduction of the standard sodium solution reversed the effect of lithium ions on the response to cutaneous nerve stimulation. The amplitude of the response attained its control value 20–30 min after sodium chloride had replaced lithium chloride.

Lithium ions have been found to replace completely sodium ions in the mechanisms which produce action potentials in squid giant axon⁶, frog skeletal muscle fibres⁷ and mammalian unmyelinated fibres⁸. Furthermore, at the amphibian neuromuscular junction, lithium chloride has the same properties as sodium chloride⁹. Similarly, Armett and Ritchie¹⁰ noted that replacing sodium with lithium ions did not modify the rate of onset and extent of the acetylcholine-evoked depolarization of mammalian unmyelinated fibres. Impulse transmission in mammalian sympathetic ganglia was blocked, however, by lithium^{11,12}. This inability of lithium to support transmission of impulses in sympathetic ganglia has been attributed^{11,12} to

impairment of postsynaptic processes. An important difference between sodium and lithium ions is the relative difficulty with which lithium is extruded from intracellular sites. In amphibian skeletal muscles, spinal motoneurons and unmyelinated nerve fibres, the metabolically dependent extrusion of lithium ions is significantly slower than that of sodium^{7,8,13}. Thus it is possible that lithium failed to support ganglionic responses to pre-ganglionic stimulation and injected ACh because the cation accumulated within the ganglion cells, causing depolarization as shown also in the heart¹⁴.

We suggest two important mechanisms by which lithium could block the evoked release of ACh from the cerebral cortex. First, the lithium ions probably interfered with the conduction of impulses in cortical neurones and, second, the exposure of the cerebral cortical tissue to a sodium-free Ringer-Locke solution probably impaired ACh release and/or synthesis. Direct evidence for the latter has been reported by Birks¹⁵, who showed that the ACh synthesis and release from mammalian sympathetic ganglia were considerably reduced in the presence of low-sodium solutions.

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Transmission of Two Subacute Spongiform Encephalopathies of Man (Kuru and Creutzfeldt-Jakob Disease) to New World Monkeys

Now that kuru and Creutzfeldt-Jakob disease have been transmitted to four species of New World monkeys, spider monkeys (*Ateles geoffroyi*), capuchin monkeys (*Cebus* sp.), squirrel monkeys (*Saimiri sciurens*), and woolly monkeys (*Lagothrix lagothica*), these more readily available animals may replace the chimpanzee in the laboratory study of these two subacute degenerative diseases of the human brain.

Both diseases have been transmitted to the squirrel monkey and to the spider monkey using 10% suspensions of human brain, inoculated intracerebrally, with incubation periods of about 2 yr. Human kuru brain suspension has caused the same disease in the capuchin monkey 45 months after intracerebral inoculation (Fig. 1). Furthermore, experimental kuru in the spider monkey has similarly been transmitted to the squirrel monkey with an incubation period of 22 months, and experimental Creutzfeldt-Jakob disease of the chimpanzee to the squirrel monkey with incubation periods of 9 and 19

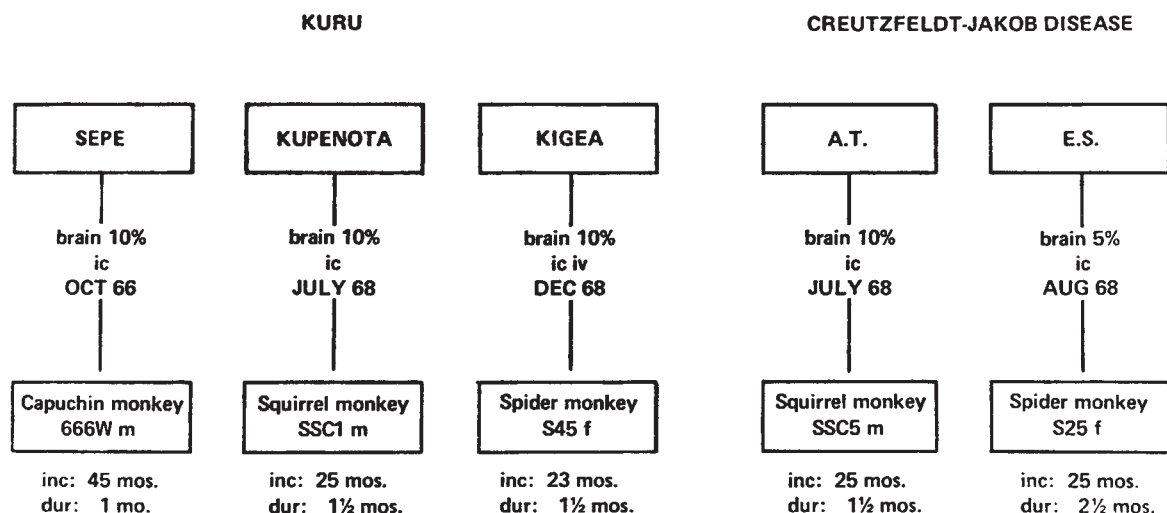


Fig. 1 Transmission of kuru and Creutzfeldt-Jakob disease to New World monkeys.

months, and to the woolly monkey after 21 months of incubation (Fig. 2). Thus, these diseases of man and the experimental diseases in the chimpanzee have now been transmitted to smaller, less expensive, more readily available and more easily cared for hosts than the chimpanzee.

Experimental kuru in the chimpanzee^{1,2} was previously passed successfully to the spider monkey³ with incubation periods of 23–28 months. It is now in third spider monkey to spider monkey passage and the incubation period on the second passage was 16 months (Fig. 2).

Kuru, known to be transmissible to the chimpanzee since 1965^{1,2}, has so far been transmitted from eleven different

human patients to eighteen chimpanzees with incubation periods of 14–39 months after intracerebral inoculation (Fig. 3). We are now in the fifth chimpanzee to chimpanzee passage and the incubation period has dropped to 10 to 18 months. Infection is possible by either intracerebral or peripheral (combined intravenous, subcutaneous, intraperitoneal and intramuscular) inoculation, and by using bacterial-free filtrates through 'Millipore' filters of 220 nm pore diameter. Both human and chimpanzee brains infected with kuru contain more than 10^6 chimpanzee infectious units per ml. Infectious virus is present in tissue pools of spleen, liver and kidney, as well as in the brains of chimpanzees affected with kuru, but

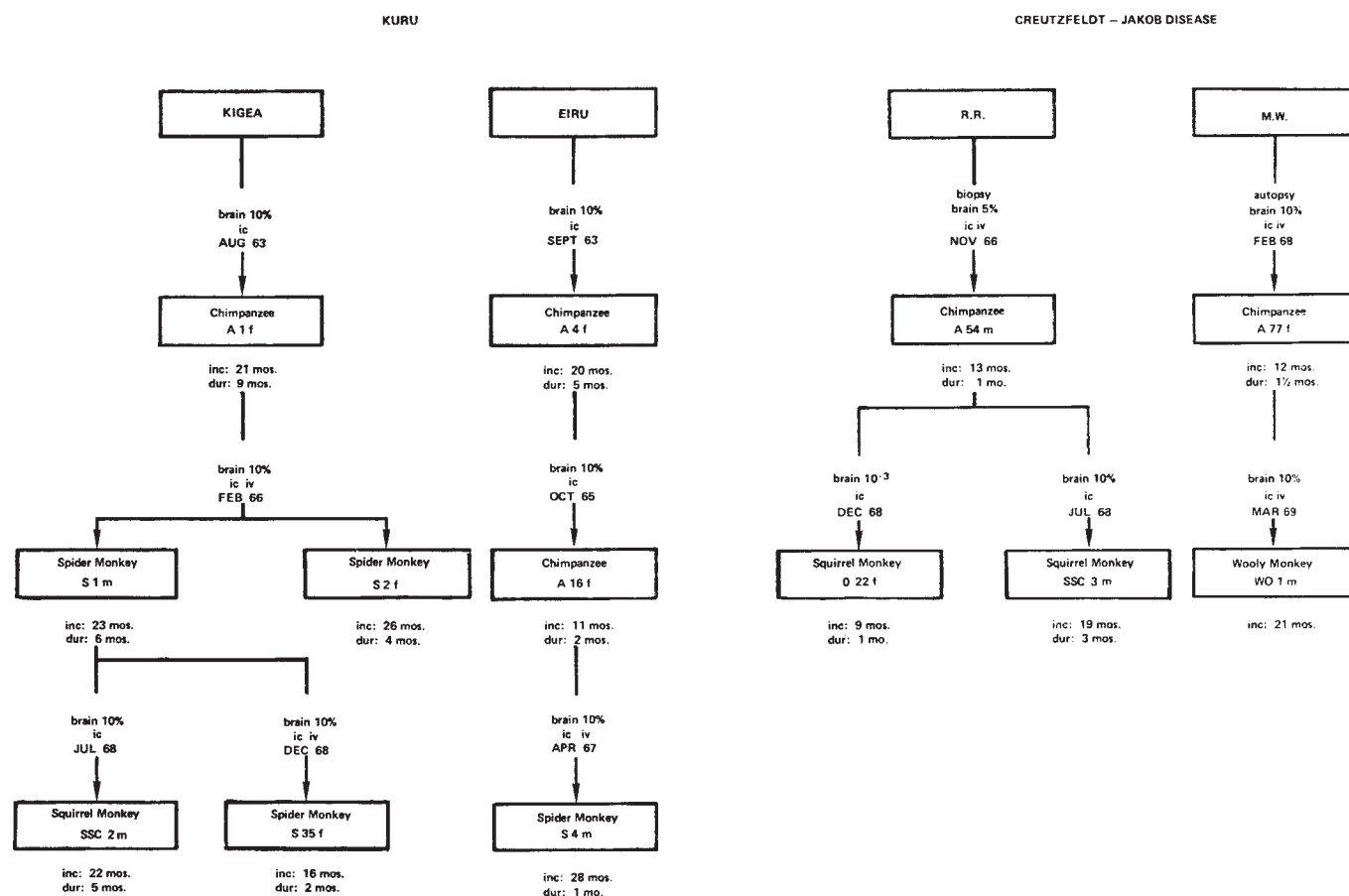


Fig. 2 Transmission of experimental kuru and Creutzfeldt-Jakob disease to New World monkeys.

so far intracerebral inoculation into chimpanzees of urine, blood, serum and cerebrospinal fluid from similarly affected humans and chimpanzees has not produced disease. Tissue suspensions of placenta and amnion from a patient who was delivered of an infant while late in her disease also failed to cause disease in the chimpanzee.

Creutzfeldt-Jakob disease was first transmitted from man to the chimpanzee in 1968^{4,5}; we have now transmitted the disease by cerebral inoculation brain tissue from ten human patients to eleven chimpanzees with incubation periods of 11–14 months. Furthermore, the brain tissue of one of these patients inoculated only peripherally (intravenously, intraperitoneally and intramuscularly) has caused the disease after 16 months of incubation. Serial passage of experimental Creutzfeldt-Jakob disease in the chimpanzee, with incubation periods of 10–14 months, has been possible using brain suspensions at dilutions of 10^{-1} and 10^{-3} .

A preliminary neuropathological survey by Dr Kenneth Earle of the Armed Forces Institute of Pathology, and Dr Peter Lampert of the University of California, San Diego School of Medicine, has revealed the presence of a gliosis, neuronal loss and status spongiosis in all the clinically positive New World monkeys, consistent with the diagnosis of experimental kuru or Creutzfeldt-Jakob disease (Fig. 4) and the detailed neuropathology of the individual animals is to be reported elsewhere (unpublished results of P. W. Lampert).

The squirrel monkey is, of course, the animal of choice for investigation of these diseases, should it be as sensitive an indicator of the viruses as the chimpanzee and if the incuba-

tion period were reduced on serial passage. In the spider monkey the incubation period of kuru was reduced from 23–28 months in first passage to 16 months in second passage. Consequently, passage of brain tissue from each affected squirrel monkey into other squirrel monkeys has been performed; and serial blind passage at 3–6 month intervals is in progress. Human brain suspension from twenty further cases of kuru and twenty of Creutzfeldt-Jakob disease has also been inoculated into New World monkeys. Titration of human and chimpanzee kuru brain suspensions known to be infectious at 10^{-5} dilution for the chimpanzee has been done in squirrel and capuchin monkeys.

To achieve a degree of isolation which is unobtainable in any single primate holding facility we have used three widely separated facilities, in California, Louisiana, and Maryland. So far, dozens of additional chimpanzees and monkeys inoculated with brain and other organ suspensions from other subacute and chronic neurological disorders have lived in each colony in close contact with animals inoculated with material from kuru and Creutzfeldt-Jakob disease. Thus far, no neurological disease has appeared in any of these "control" animals, which further serves to indicate that experimental kuru and Creutzfeldt-Jakob disease are not communicable.

The squirrel, spider and capuchin monkeys and the chimpanzee are the only species out of twenty-three sub-human primates to develop kuru after inoculation with tissues from human kuru victims. Creutzfeldt-Jakob disease has been transmitted directly with human tissues to the squirrel and spider monkeys, as it was transmitted earlier to the chimpan-

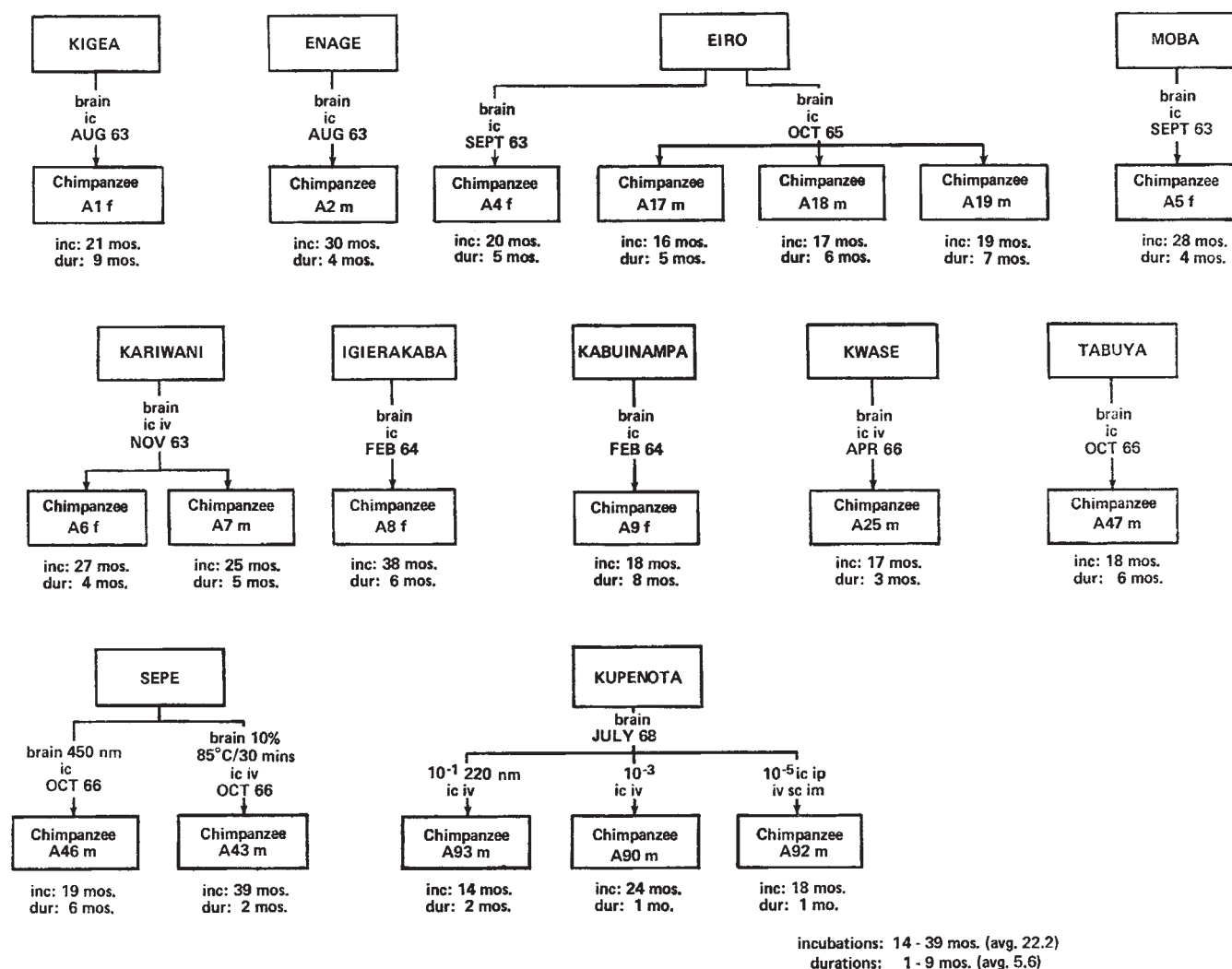


Fig. 3 Primary transmission of kuru from brain tissues of eleven human patients to eighteen chimpanzees.

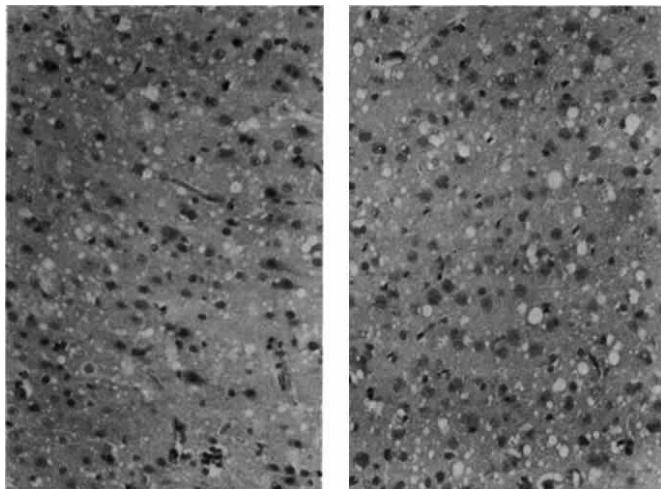


Fig. 4 Spongiform changes in the cerebral cortex of two squirrel monkeys: on the left (squirrel monkey SSC-1 in Fig. 1) inoculated with brain suspension from a kuru patient, and, on the right (squirrel monkey SCC-5 in Fig. 1), inoculated with brain suspension from a patient with Creutzfeldt-Jakob disease.

zee. Furthermore, experimental Creutzfeldt-Jakob disease of the chimpanzee has been transmitted to the woolly monkey (Fig. 1). With the exception of the chimpanzee, none of the sixteen Old World species including the gibbon ape, and in addition the two other species of New World monkeys that were used*, has developed clinical disease after intracerebral inoculation with brain suspensions from patients suffering from kuru or Creutzfeldt-Jakob disease and from chimpanzees in which these diseases have been induced. The successful transmission of both the natural human and the experimental chimpanzee diseases into the squirrel monkey has therefore provided a new laboratory model, more convenient than the chimpanzee, for the study of these diseases.

We have no explanation for the susceptibility of the three species of New World monkeys to kuru, and the three species of these monkeys to Creutzfeldt-Jakob disease, whereas all the Old World monkeys studied have been resistant. There is still need for attempts to discover a broader host range for these slow virus infections in the hope that laboratory investigations may be further facilitated. In this regard it may be noted that our attempts to transmit both diseases to some thirty other mammalian and avian hosts by intracerebral inoculation of brain suspensions have been unsuccessful so far. But, in view of the finding of minimal kuru-like neuropathology in some inoculated animals dying without clinical neurological disease, we are involved in a further programme of blind passage in the species under suspicion.

Eckroade *et al.*⁶ have successfully transmitted mink encephalopathy to the squirrel and stump-tailed monkey. This disease and scrapie are the two naturally occurring diseases which we have grouped with kuru and Creutzfeldt-Jakob disease and called subacute spongiform virus encephalopathies⁷. Scrapie virus has not yet produced clinical disease in a primate and, although sheep, goat and mouse strains of this

* Species used in transmission attempts were six New World monkeys: squirrel monkey (*Saimiri sciurens*), capuchin monkey (*Cebus* sp.), spider monkey (*Ateles geoffroyi*), woolly monkey (*Lagothrix lagothricha*), owl monkey (*Aotus trivirgatus*), and marmoset (*Callithrix* sp.); fifteen Old World monkeys: rhesus monkey (*Macaca mulata*), cynomolgus macaque (*M. irus*), stump-tailed macaque (*M. speciosa*), bonnet monkey (*M. radiata*), barbary ape (*M. sylvana*), pig-tailed macaque (*M. nemestrina*), African green monkey (*Cercopithecus aethiops* sp.), baboon (*Papio anubis*), langur (*Colobus* sp.), sooty mangabey (*Cercocebus atys*), patas (*Erythrocebus patas*), slow loris (*Nycticebus coucang*), talapoin (*Cercopithecus miopithecus*), tree shrew (*Prilocercus lowii*), and bush baby (*Galago senegalensis*); two apes: chimpanzee (*Pan troglodytes troglodytes*) and gibbon ape (*Hylobatus lar*).

virus have been inoculated into many species of monkeys and into the chimpanzee, all animals have remained well for periods of 3 to 5 yr. Reports of the transmission of scrapie to mink and of mink encephalopathy to goats and mice⁸⁻¹⁰ reinforce the suspicion that the agents of these diseases are closely related. The crucial question of whether the viruses of kuru and Creutzfeldt-Jakob disease are related cannot be answered until serological identification of the viruses is possible and more is known of their properties. Whether one or both are related to the viruses of the two pathologically similar animal diseases remains to be determined.

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Infection of Mammalian Unfertilized and Fertilized Ova with Oncogenic Viruses

REPORTS on the infection of mammalian ova with viruses¹⁻³ chiefly concern the exposure of ova to cytolytic viruses, such as those causing Mengo encephalitis or vesicular stomatitis. We have investigated the effect of two oncogenic viruses, which do not usually destroy infected somatic mouse cells, on unfertilized and fertilized mouse ova.

Unfertilized ova were obtained from either 8-10 week old Swiss or C57Bl/6 virgin mice by a standard technique⁴. Cells were separated from corona radiata by treatment with hyaluronidase, and the zona pellucida was removed by treatment with pronase, as described previously⁴. (The viruses tested were not capable of penetrating fertilized or unfertilized eggs with intact zonae pellucidae.) Fertilized ova were obtained from Swiss ICR mice superovulated by injection of 0.4 IU g⁻¹ of serum gonadotropin, followed 2 days later by 0.4 IU g⁻¹ of chorionic gonadotropin. Immediately after the second injection, the mice were mated. Those with vaginal plugs were killed after 2 or 4 days, and the two celled or morula ova flushed from the oviducts.

The ova were infected with the Rh 911 strain of simian virus 40 (SV40) grown in CV-1 cells, infectious SV40 DNA extracted from purified virus preparation⁵, or Moloney sarcoma virus (MSV) grown in BALB/c mouse embryonic fibroblasts. Usually fifty to a hundred unfertilized and two celled fertilized ova and twenty to forty morulae were exposed either to 10⁶ plaque-forming units (p.f.u.) of SV40, 0.2 µg of SV40 DNA (suspended in 0.5% dimethylsulphoxide in Brinster's medium (BMCO₂)⁶, or to 2 × 10³ p.f.u. of MSV diluted with BMCO₂ or Whitten's medium (WMCO₂)⁷, for 1 h at 37° C. After

Table 1 Effect of Oncogenic Virus Infection on Unfertilized Mouse Ova

Virus	No. of ova infected	No. showing "fragmentation" or developing to two or more celled stage, with or without nuclei
SV40	60	20
SV40 DNA	60	45
MSV	364	71
None	60	42

adsorption, unfertilized and fertilized ova were washed three times in BMCO₂ or WMCO₂. Those exposed to SV40 were treated with SV40 antibody-containing rabbit serum, and those exposed to SV40 DNA with DNAase 1. Ova exposed to MSV were treated with anti-MSV serum.

The virus was isolated from unfertilized or fertilized ova exposed to either SV40 or SV40 DNA by placing the cells, 48–72 h after infection, in direct contact with CV-1 cells⁸ in the wells of Terasaki plates⁴. We used the same technique to isolate MSV, except that Rous sarcoma virus-transformed XC rat cells⁹ were placed in direct contact with the infected unfertilized and fertilized ova. The Terasaki plates were incubated at 37° C in a 5% CO₂ atmosphere. The CV-1 cells were examined daily for cytopathic lesions characteristic of SV40 infection, and the XC cells were examined for the presence of syncytia characteristic of MSV infection⁹.

number of blastulae which yielded virus after infection during the morula stage with either SV40 or SV40 DNA was slightly, but not significantly, lower. From the formation of syncytia from XC cells, we concluded that most of both the unfertilized and fertilized ova infected with MSV yielded infectious virus. (Polyoma virus seems to destroy all unfertilized eggs within 24 h after exposure.)

Table 3 Isolation of Virus from Virus-exposed Ova

Virus	Ratio of unfertilized or fertilized ova causing cytopathic effect* on CV-1 cells or syncytiogenic effect* on XC rat cells		
	Unfertilized ova	Fertilized ova infected as: Two celled ova	Morula
SV40	28/36	50/90	10/22
SV40 DNA	38/48	Not tested	12/25
MSV	54/104	10/13	23/32

* Unfertilized and fertilized ova infected at two celled stage were checked for virus production 72–96 h after exposure; morula were checked 24 h after exposure.

We have shown that after exposure of unfertilized and fertilized ova at various stages of development *in vitro* to two oncogenic viruses—SV40 and MSV—and to DNA extracted

Table 2 Effect of Oncogenic Virus Infection on Fertilized Ova

Virus type	Virus infection Stage of development at time of infection	No.	No. degenerated	No. of developing ova observed 72 h after infection				
				Two celled	Four celled	Six to eight celled	Morula	Blastula
SV40	Two celled ova	252	32	21	40	47	73	39
	Morula	22	—	—	—	—	—	22*
SV40 DNA	Two celled ova	180	81	63	15	18	3	0
	Morula	25	—	—	—	—	—	25*
MSV	Two celled ova	45	—	12	9	9	8	7
	Morula	32	—	—	—	—	—	32*
None	Two celled ova	44	—	13	6	11	5	9

* Observed 24 h after infection.

The exposure of unfertilized ova to infection with the two viruses or SV40 DNA had little, if any, deleterious effect. Only a few ova in each experimental group underwent actual degeneration during the 72 h observation period, and many ova showed changes which have been described in Table 1 as "fragmentation", which refers to the formation from one ovum of four to twenty microfragments of cytoplasm, and presumably nucleus, usually within 24 h of cultivation *in vitro*.

As well as fragmentation, we observed individual ova which developed to the two to eight celled stage, some of which contained distinct nuclei. The percentage of these parthenogenetically developing cells was slightly higher for ova exposed to SV40 DNA than for uninfected ova, but too few observations were made for any definite conclusions to be drawn.

Table 2 shows the effect of viral infection on the development of fertilized ova. As for unfertilized eggs, there was no evidence of a deleterious effect of either SV40 or MSV infection on the development of the ova in culture. The deleterious effect of SV40 DNA on two celled ova may be more apparent than real, because the toxicity of DNA may be related to the presence of dimethylsulphoxide in the inoculum. None of the morulae exposed to virus or to SV40 DNA were affected, however; all developed to the blastula stage.

Infectious virus was isolated from unfertilized and fertilized ova at the two celled and morula stages (Table 3). After exposure to either SV40 or SV40 DNA (unfertilized ova only), more than half the unfertilized and two celled ova, when placed in contact with CV-1 cells, yielded infectious SV40. The

from SV40, infectious virus can be isolated from the ova in suitable culture systems. Viral infection did not have a deleterious effect on the ova, which developed *in vitro*. (We are investigating the effect on *in vivo* development beyond the blastula stage of the early infection of fertilized ova with oncogenic viruses.)

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Distribution of Marihuana in Monkey Brain and Concomitant Behavioural Effects

MARIHUANA and hashish have been used for centuries and the literature abounds with references to their effects. Only recently, however, have carefully controlled studies attempted to relate dose level and route of administration of Δ^9 -tetrahydrocannabinol (Δ^9 -THC), the principal psychoactive constituent of *Cannabis sativa*, to subjective and objective physiological, behavioural and mental effects¹⁻³. Attempts have also been made to compare the effects of Δ^9 -THC with those of ethanol⁴.

We have studied the distribution in the central nervous system of an extensive series of psychotropic agents by autoradiography and found evidence of their site of action (refs. 4, 5 and B. T. Ho, G. E. Fritchie, J. E. Idänpään-Heikkilä, W. M. McIsaac and L. W. Tansey, in preparation), and felt that a similar study of Δ^9 -THC would be timely.

The two principal obstacles to such a study was the provision of radioactively labelled Δ^9 -THC of a sufficiently high specific activity which would penetrate the brain. We overcame the first difficulty by synthesizing Δ^9 -THC with a specific activity of 250 $\mu\text{Ci}/\text{mg}^{6-8}$. The Δ^9 -THC (>90% purity) was then separated using 'Florisil' column chromatography. The authenticity of our synthetic Δ^9 -THC and Δ^8 -THC was established by retention times (gas chromatography) and R_F value (thin-layer) chromatography compared with standards of Δ^8 -THC and Δ^9 -THC (as the principal constituent of red oil) provided by Dr Sciliagno of the National Institute of Mental Health and synthetic Δ^8 -THC and Δ^9 -THC provided by Dr L. Hines of Hoffmann-La Roche. The second problem was overcome by using the intravenous route for administration. Our preliminary findings indicate that very little Δ^9 -THC is absorbed after intraperitoneal injection, and it would have been virtually impossible to get sufficient brain accumulations for autoradiography using this route.

Table 1 Regional Localization of ^3H - Δ^9 -THC in Monkey Brain after Intravenous Administration

Brain area	Radioactivity ($\mu\text{Ci}/\text{g}$)					
	2 mg/kg		30 mg/kg		24 h	
	15 min	4 h	15 min	1 h	4 h	
Frontal cortex	0.63	0.38	6.45	4.61	2.56	0.26
Frontal white	0.42	0.26	1.17	4.21	2.60	0.41
Parietal cortex	1.05	0.23	5.28	5.16	1.44	0.36
Parietal white	0.26	0.15	1.85	1.81	1.95	0.30
Corpus callosum	0.13	0.15	2.61	4.20	1.72	0.56
Visual cortex	1.32	0.16	6.74	4.32	1.63	0.22
Caudate	0.66	0.23	5.89	6.04	1.42	0.14
Putamen	0.50	0.18	3.92	4.17	1.79	0.35
Optic tract	0.30	0.08	0.54	1.42	0.95	0.33
Geniculate nuclei	0.75	0.17	4.06	5.50	2.82	0.49
Hypothalamus	0.51	0.14	1.85	3.22	1.91	0.17
Hippocampus	0.45	0.18	4.48	6.02	2.31	0.40
Cerebellar cortex	0.49	0.31	6.64	10.73	2.06	0.51
Pituitary gland	0.28	0.07	3.68	1.75	0.40	0.19
Pons	0.45	0.22	4.76	6.64	1.92	0.61
Medulla	0.53	0.19	4.17	6.53	1.94	0.39
Thalamus	0.57	0.21	5.48	7.05	2.39	0.46
(Plasma)*	1.76	0.13	9.98	5.71	2.88	1.10

* $\mu\text{Ci}/\text{ml}$.

Six male and two female squirrel monkeys were given doses of 2 mg/kg (two), 10 mg/kg (two) or 30 mg/kg (four) of ^3H - Δ^9 -THC, through the femoral vein without anaesthesia. The general behaviour of the animals was observed and they were bled to death 15 min or 1, 4 or 24 h after injection. Half of each brain was used for autoradiography (Fig. 1) as described before^{9,10}. The remaining hemispheres and the brains from the low dose animals were dissected; the samples were homogenized in methanol or benzene and were assayed for tritium by liquid scintillation (Table 1). Unchanged ^3H - Δ^9 -THC

content of the whole brain was analysed by chromatography. Total brains were homogenized in five parts benzene, centrifuged and the supernatant (plus subsequent washings) was concentrated for chromatographic identification. Δ^9 -THC was identified by its R_F (thin-layer chromatography; hexane; diethyl ether (4:1)), a positive colour reaction to *ortho*-dianisidine-tetrazolium chloride, and its retention time (gas chromatography columns: 3% OV-17 on 'Chromasorb W' and 3% SE-30 on 'Varaport 30'). The percentage unchanged was determined as percentage of radioactivity localized as Δ^9 -THC.

With a dose of 2 mg/kg the animals sat quietly, staring at the bottom of the cage taking little notice of their surroundings or the investigator. Their normal aggressive response to handling disappeared under the influence of the drug. At 10 mg/kg, there was an initial period of stimulation during which the animals appeared excited: jumping, turning, and freezing in awkward catatonic-like positions. Marked motor incoordination was also obvious. During this period the animals gazed about the room, not focusing, as is usually the case, on the experimenter. The behaviour was such that it was tempting to infer that the monkeys were hallucinating. At 30 mg/kg, there was marked sedation and pronounced motor incoordination which was maximal at 1 h. These effects subsided within 8 h, leaving the animals with a tendency to overreact to external stimuli.

Two factors relating to the mode of action of the Δ^9 -THC in the brain must be considered: first, the amount of unchanged Δ^9 -THC present at various times, and second, the differential distribution in various cortical and subcortical structures.

It has been reported that maximal effects in man are evident within 15 min and endure for 4-6 h, and so it is significant that we estimated 77% of the radioactivity present in the brain 15 min after administration was due to unchanged Δ^9 -THC; this value had declined to 51% at 4 h. This decline in Δ^9 -THC in 4 h paralleled the diminution of behavioural effects which we noticed in our monkeys, which were similar to those reported in detail by Scheckel *et al.*¹¹. Although they used larger doses to obtain the same effects, this could be explained by the difference in route of administration.

Much of the behavioural effect may well be related not only to the distribution of Δ^9 -THC in the brain, but also to changes in this distribution pattern at different times.

Within 15 min, at all doses, neocortical areas contained high concentrations of Δ^9 -THC (Fig. 1A and B; Table 1). This was most marked in the frontal cortex. In contrast, there was very little in the white matter, which is somewhat surprising in view of the lipophilic nature of Δ^9 -THC. We have recently noted a similarly high ratio of concentration in grey as compared with white matter when ^{14}C -1-ethanol was studied⁴. Another similarity between Δ^9 -THC and ethanol is the marked accumulation in the cerebellum, fastigial, and dentate nuclei which may be related to the motor incoordination produced by both agents.

Fifteen minutes after Δ^9 -THC administration, lateral and medial geniculate nuclei had a high level of radioactivity. The lateral geniculate is known to have connexions with the visual pathway, and so the fact that it contained the highest concentration at a time when visual perception was most distracted and when the behaviour suggested that the animals were hallucinating might indicate one locus of action. Similarly high concentrations were seen in the amygdala, hippocampus, inferior and superior colliculi when the behaviour observed concomitantly included mild sedation and tranquillization at low dose, excitation and distracted behaviour at medium dose and marked sedation and gross motor incoordination at high dose.

Other structures with a high concentration include the caudate nucleus, putamen and pons. The anterior commissure, optic tract, internal capsule and pyramidal tract, on the other hand, had extremely low concentrations of activity.

Plasma levels of radioactivity were significantly lower than regional brain concentrations only at 4 h (2 mg/kg) and 1 h

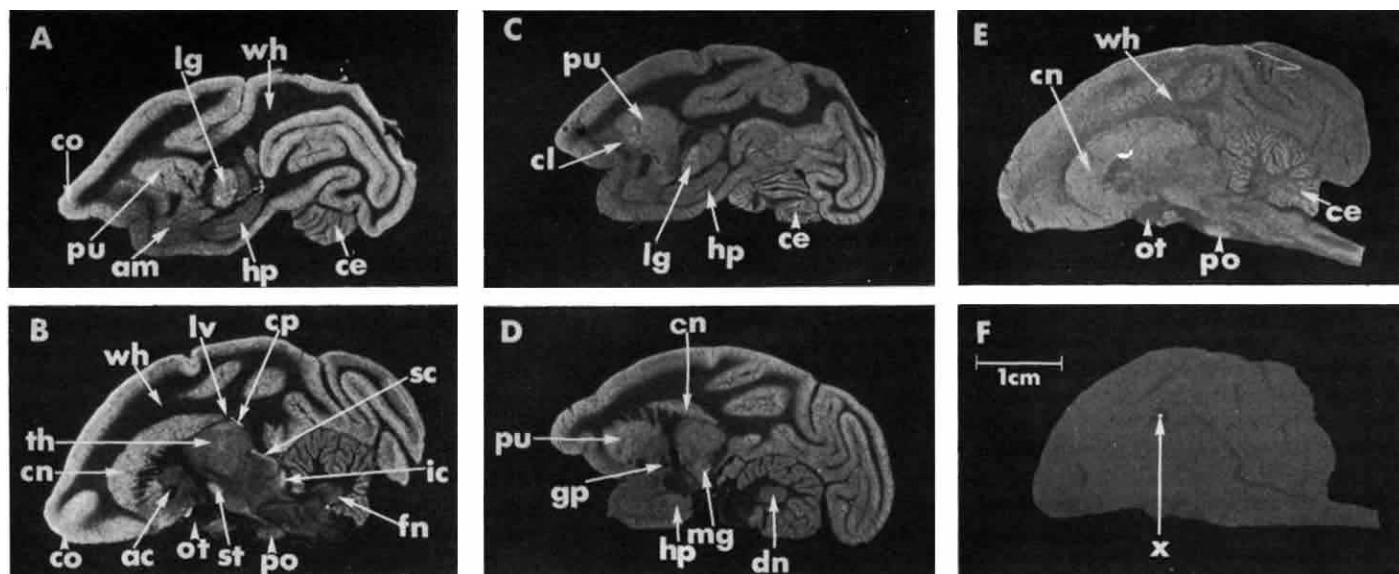


Fig. 1 Distribution of radioactivity (light areas) in monkey brain 15 min (A, B), 1 h (C, D), 4 h (E) and 24 h (F) after intravenous injection of ^3H - Δ^9 -THC. ac, Anterior commissure; am, amygdala; ce, cerebellum; cl, claustrum; cn, caudate nucleus; co, cortex; cp, choroid plexus; dn, dentate nucleus; fn, fastigial nucleus; gp, globus pallidus; hp, hippocampus; ic, inferior colliculus; lg, lateral geniculate nucleus; lv, lateral ventricle; mg, medial geniculate nucleus; ot, optic tract; po, pons; pu, putamen; sc, superior colliculus; st, subthalamic nucleus; th, thalamus; wh, white matter; x, artefact.

(30 mg/kg, Table 1). It has been shown that permeability of the blood brain barrier, blood flow, and vascularity affect accumulation of drugs in the brain¹²⁻¹⁴. Although the site of accumulation of a drug does not necessarily prove its locus of action, we found distinct concentrations which could be readily related to the behavioural, physiological and mental effects produced by Δ^9 -THC^{1-3,12}.

The hypothalamus accumulated only a small amount of radioactivity. There is thus an obvious difference between this agent and STP, which we found in high concentration in this area⁵. This may well account for the diametrically opposed behavioural effects of these two compounds: the normally mildly aggressive squirrel monkey becomes completely un-aggressive under the influence of Δ^9 -THC and violently aggressive under the influence of STP. The amygdaloid accumulation of Δ^9 -THC (and/or metabolites) may be related to its reported anxiolytic and euphoric effect in man.

We have examined the distribution in the central nervous system of a large series of psychoactive drugs and the extremely high concentration of Δ^9 -THC in the frontal cortex seemed to be unique and this, together with the hippocampal accumulation, makes it tempting to suggest that the interaction between these two areas plays an important part in associating stimuli into a temporal context. It is well known that one of the chief effects of marihuana is distortion of time perception. The frontal cortex is a general association area and Turner has hypothesized that a hippocampal function is related to imprinting and early recall of memories by superimposing temporal orientation on engrams¹⁵. Thus the pathognomonic time disruptive effect of Δ^9 -THC could well be attributed to its unique distribution in the central nervous system.

The distribution at 1 h showed a marked decline in concentration in the grey matter (Fig. 1C and D). This became increasingly evident at 4 h (Fig. 1E). Twenty-four hours later the little activity that was left was evenly distributed throughout the brain (Fig. 1F), by which time all behavioural effects had subsided.

In summary, the dose response relationship which we noted in squirrel monkeys parallels the reports of users and experimental subjects that low doses of marihuana have an anxiolytic and euphoric action accompanied by disruption of time perception; medium doses cause stimulation and talkativeness; higher doses are hallucinogenic, and very high doses cause incapacitation of cognitive and motor function. Thus these objective and subjective observations of the behavioural

effects of marihuana and its psychoactive constituent Δ^9 -THC indicate a strong relationship between its distribution in the brain, rate of metabolism, and its actions.

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Observed and Predicted ^{90}Sr and ^{137}Cs Levels in Milk

A RELATIONSHIP between the radioactive contamination of milk, the rate of fallout and the deposit on soil has been suggested by Tajima¹. $C = prFr + pdFd$, in which C is the mean annual contamination of milk (pCi ^{90}Sr /g Ca), Fr is the annual deposit (mCi ^{90}Sr /km²), Fd is the cumulative deposit of ^{90}Sr (mCi ^{90}Sr /km²) and pr , pd are the proportionality factors related respectively to Fr and Fd .

In the United Kingdom, the data provided from an extensive country-wide survey led Bartlett *et al.*² to introduce a third term into this equation, which becomes $C = prFr + plFl + pdFd$ where Fl is the deposit in the last half of the previous year and pl is the "lag-rate" factor.

As Stievenart *et al.*³ emphasize, the numerical values of proportionality factors mentioned in the literature are very disparate and hardly comparable, because of the choice of the different periods. It therefore seemed interesting to investigate whether, in the case of milk collected in Belgium during 1964–1969, the prediction formulae and the numerical values of proportionality factors (Table 1) suggested by Euratom³, the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) modified by Euratom³, and by Bartlett and Russell² gave values for C in agreement with observation. The figures used for the determination of Fr and Fd are those of the fallout measured in Mol^{4–8}, the observed level of contamination in milk, obtained from a country-wide survey of the radiocontamination of the food chain in Belgium^{9,10}.

Table 1 Prediction Formulae for Milk Contamination (Year n)

Terms of equation	Euratom	UNSCEAR	United Kingdom
C (12 months mean ratio pCi ^{90}Sr /g Ca of pCi ^{137}Cs /l. in milk)	1 May n –30 April $n+1$	1 Jan n –31 Dec n	1 Jan n –31 Dec n
Fr (annual deposit)	1 April n –30 Sept n	1 Jan n –31 Dec n	1 Jan n –31 Dec n
Fl (deposit in last half $n-1$ year)			1 July –31 Dec $n-1$
Fd (cumulative deposit)	31 March n	30 June n	30 June n
pr (rate factor) ^{90}Sr ^{137}Cs	1.95 7.01	0.95 4.48	0.70 3.00
pl (lag-rate factor) ^{90}Sr ^{137}Cs	— —	— —	1.13 6.00
pd (soil factor) ^{90}Sr ^{137}Cs	0.26 1.03	0.23 1.27	0.11 0.03

For 1964–1969, the Euratom formula gives the smallest difference between the predicted and observed values for ^{90}Sr . The formula of UNSCEAR, used with proportionality factors recounted on the whole of the data observed in the countries of Euratom, gives higher values, especially since 1967, because of the excessive contribution of the "soil factor", pd . Russell *et al.*¹¹ found a similar disagreement between the values

predicted, respectively, by the methods of UNSCEAR and Bartlett *et al.*²; the cause could be the loss of ^{90}Sr through the leaching of the rooting zone and the grazing of the grass, which are under-estimated in the UNSCEAR formula. According to Stievenart *et al.*³, the quantity of ^{90}Sr in the rooting zone would diminish by about 5% per year. We find good agreement between the formulae of Euratom and the United Kingdom on the percentage of contamination attributable to uptake from soil in Belgium.

The use of the Euratom formula gives predicted values systematically higher than those observed for ^{137}Cs whereas the United Kingdom formula gives the reverse; the biggest variations appear in 1965. The cause of this discrepancy is not the value of $prFr$: the contribution of the direct retention of ^{137}Cs by grass is about 47% if the Euratom formula is used, and about 38% with the United Kingdom formula for 1964–1969. Concerning the contribution of the indirect contamination, Bartlett *et al.* distinguish between uptake of ^{137}Cs by the roots of the grass, which is of little importance and leads to a low value for pd , and the uptake of ^{137}Cs from the "mat", in which case the ^{137}Cs remains available during the months which follow a deposit. It results in the high value for pl (lag-rate factor). Stievenart *et al.*³ do not make this distinction. They used a high value for pd but they apply to Fd a reduction coefficient (0.55) in such a way that $pdFd$ reflects mostly the lag-rate phenomenon due to the "mat".

Several publications dealing with the radioactive contamination of the environment by world-wide fallout have pointed out that the correlation between the deposition of activity and the resulting levels in milk was not always clear, because of the number of factors involved. Among them, we emphasize the importance of the climatic and soil conditions, which influence the yield of the pasture and the level of grass contamination. The use of the prediction formula suggested by the Euratom and United Kingdom experts gives a good agreement (5%) between the predicted and observed levels of ^{90}Sr in milk collected in Belgium. The UNSCEAR formula gives values which are too high (27% for 1964–1969). As for ^{137}Cs , the Euratom and United Kingdom formulae give, respectively, values which are too high and too low—about 20% for the whole period considered. The UNSCEAR formula gives values of about 12% too low. Finally, large variations have been observed related to the type of soil and the quality of pasture. In the case of ^{137}Cs , some milk has a level of contamination four times higher than the country-wide mean; for ^{90}Sr , the maximal variation is 1.5 times.

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Radiation-induced Light Flashes observed by Human Subjects in Fast Neutron, X-ray and Positive Pion Beams

ASTRONAUTS on Apollo 11, 12, and 13 observed a series of light flashes and streaks when they were in darkness at great distances from the Earth¹. Although it is well known that relatively low doses of X-rays impinging on the retina can cause light sensation and can alter the light sensitivity threshold², the astronauts' descriptions of discrete flashes and streaks do not conform with the homogeneous flood of light which is characteristic of X-ray phosphores or the crescents and patterns of electrical or pressure phosphores.

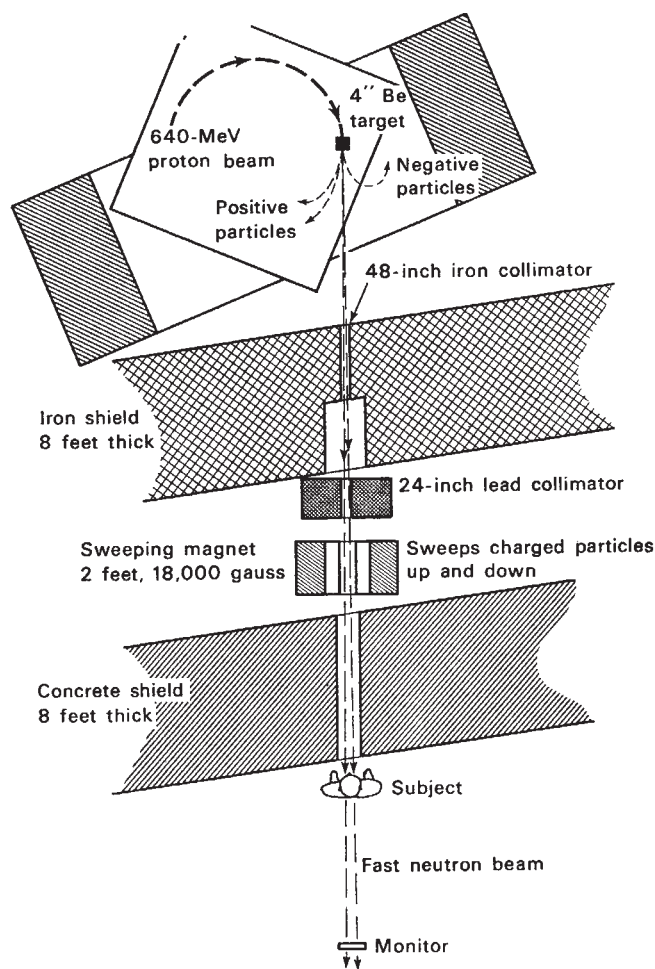


Fig. 1 Configuration used at the 184 inch cyclotron for fast neutron exposures in the region of the human eye.

So it is possible that these flashes are caused by ionization or some other form of interaction of primary cosmic particles with tissues, as predicted³ in 1952. The streaks might be heavy primaries, and double points could be accounted for by one cosmic particle intersecting the retina at two points. To test the validity of these hypotheses and the probability that the human dark-adapted eye may be a sensitive and unique cosmic ray detector, we have investigated visual phosphene phenomena produced by fast neutrons (maximum 0.64 GeV) at the Berkeley 184 inch cyclotron. The range of recoil atoms and nuclear fragments is much less than that for primary cosmic ray particles but the biological effects are probably qualitatively similar. Our experiments also included exposures with

π^+ mesons at the Berkeley bevatron and low energy (<25 MeV) neutrons.

Two human subjects were exposed to a beam of fast neutrons with energies between 20 and 640 MeV produced by a 0.64 GeV proton beam impinging on a 12 cm beryllium target. Most of the neutrons were at energies near 300 MeV and only 2% or less of the dose came from slow neutrons and gamma rays. The flux, continuously monitored, was 1.4×10^4 neutrons $\text{cm}^{-2} \text{s}^{-1}$. Neutrons were collimated and channelled by a set of iron and lead apertures 2 m thick (Fig. 1) so arranged that charged particles were either deflected away or absorbed. The neutrons formed a narrow beam (6.5×5.2 cm) entering a shielded room. We used frontal exposures in which the beam went through one eye (Fig. 1) and lateral exposures in which both eyes were exposed. The dose rate⁴ in the path of the beam was 1 mrem s^{-1} . The integrated doses for our two subjects were 8.5 mrem (for C.T.) and 2.6 mrem (for T.B.) respectively, which were less than the smallest doses received by the chest in routine diagnostic chest X-ray examination and much less than the permissible weekly exposures for the United Kingdom or the United States.

The subjects were adapted to the dark by wearing a combination of green sunglasses and red X-ray dark-adapting glasses for more than 2 h before exposure. During the last 15 min, all light was excluded by a black hood covering the entire head and neck, a procedure considered more than adequate for the usual dark-adaptation and visual threshold experiments.

On four exposures of between 1 and 3.5 s, subject C.T. saw pinpoint flashes coinciding with the presence of the beam. These were described as small scintillations similar to the luminous balls seen in fireworks, with initial tails fuzzy and heads like tiny stars. These pinpoints of bright light appeared to be moving and to be much brighter than the occasional dim pinpoints of light seen while resting in a dark-adapted state. Subject T.B. received one 3 s exposure after only 10 min of full dark-adaptation, and saw between twenty-five and fifty bright discrete lights, which he described as stars, blue-white in colour, coming towards him (Fig. 2). This was a definite effect clearly associated with the presence of the neutron beam, and very unlike X-ray phosphores or electrical phosphores also experienced by subjects in other experiments.

In a later 6 s exposure at the bevatron with 1.5 GeV/c momentum π^+ mesons, the flux was 200 particles $\text{cm}^{-2} \text{s}^{-1}$, with a total absorbed dose to the head of 0.2 mrem. The beam contained no protons or other particles. The dark-adapted subject (T.B.) noted no visual phenomenon during, or after, a total exposure of about 5,000 particles through each retina. Any interactions in the eye or Čerenkov-effect photons were not sufficiently intense or concentrated to be detected.

X-ray phosphores were investigated in order to compare their characteristics with those of the neutron beam phosphores, and also to find out whether X-ray phosphores can be produced at the maximum dose rate possible (0.1 mr s^{-1}) of incidental X-rays or gamma rays during the neutron exposures. The X-ray phosphene phenomenon is a function of dose rate and is easily noticeable at dose rates greater than 24 mr s^{-1} , the exposures usually encountered in routine clinical X-ray work. The light sensation is described as a soft bluish-grey or white diffuse light across the visual fields of both irradiated eyes and is said to be similar to an atmospheric electrical discharge behind clouds on the horizon. At dose rates up to 1.25 mr s^{-1} for exposures up to 10 s, no visual phenomena similar to the bright pinpoints of light observed during neutron exposure were seen by the experimental subjects. This dose rate is ten times greater than that from incidental X or gamma rays during neutron exposures.

The possible causes of the light flashes include ionization from products of non-elastic collision and high energy recoils on carbon, nitrogen, and oxygen in and near the retina, ionization excitations from proton recoils in or near the retina and Čerenkov radiation. The number of recoil atom interactions

is estimated to be 43 per second in one eye, assuming a mean range of 500 μm , but this calculation could be in error by a factor of 100, for the range may be less than 500 μm . Twenty-five to fifty events were observed during exposures of 3 s by both individuals. A calculation using a proton range of 2 cm gives the number of proton events in each eye at 370 per second. It is very unlikely that recoil protons are involved in the production of bright pinpoints of light, as neutrons (1 MeV maximum abundance) at a flux of $10^5 \text{ cm}^{-2} \text{ s}^{-1}$ for more than 12 s, using californium-252 gave no definite flash-like phenomenon while 1.5 GeV/c π^+ mesons do not produce light flashes in the retina.

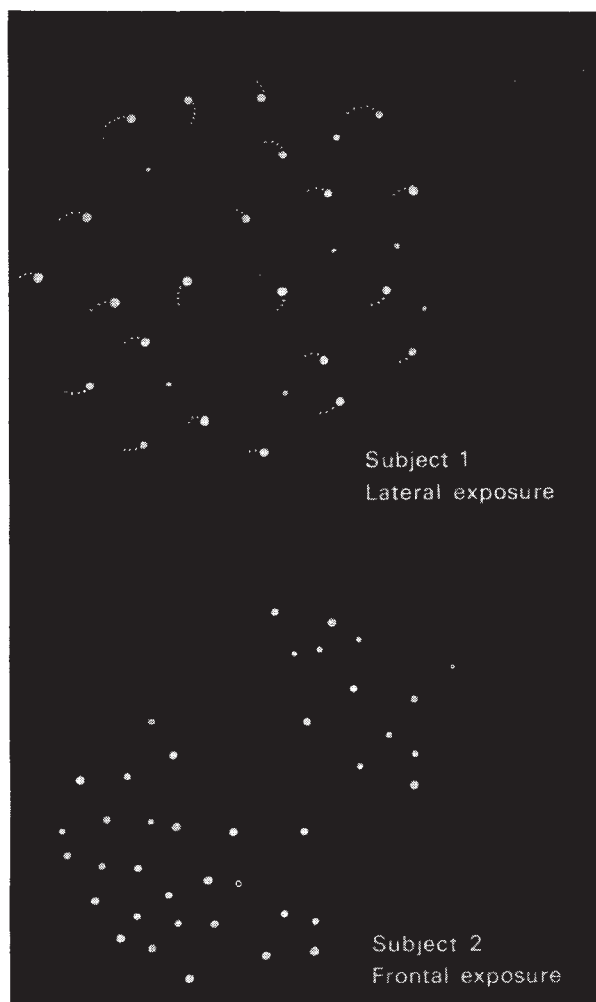


Fig. 2 Subjects' representations of size, shape and abundance of the white flashes seen during and after exposure to a neutron beam laterally through both eyes, and on anterior-posterior exposure through one eye.

We are also doubtful that the Čerenkov effect from recoil protons caused the scintillations in this experiment. Contrary to the statistical conclusions of D'Arcy and Porter⁵, we have not been able to see flashes at ground level, or in an aircraft at 10,000 m, which could be attributable to cosmic ray mesons. Because lower energy neutrons (4–12 MeV) caused similar, definite star-like flash phenomena in experiments with five dark-adapted patients who underwent whole body neutron activation⁶, and in earlier experiments by Fremlin⁷, this Čerenkov effect is unlikely to be the principal mechanism for these flashes⁸. Considering the lack of effect at lower energies of the ^{252}Cf fission neutrons (maximum abundance at 1 MeV), alpha particles from the (n, α) reaction on N, C, and O can probably cause the effect we observed. The Čerenkov effect could contribute to the light flashes seen by astronauts in space, where the observed frequency of events correlates with

the expected flux of heavy cosmic ray primaries with atomic numbers of carbon and higher.

Inside the human head the retina is the probable locus of interaction with radiation⁴. If the action of particles is a result of ionization or excitation, it seems likely that the particles must pass through the light-sensitive cells (that is, the rods) that they affect.

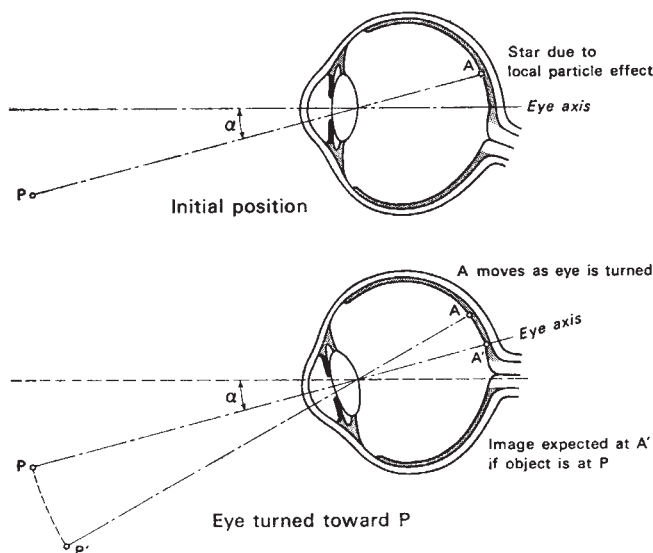


Fig. 3 A flash at A on the retina may cause the illusion that there is a luminous source at point P external to the subject. The subject instinctively turns his eyes towards P; during these eye movements the location of the source appears to recede to P' as light sensation fades. The subject thus has the subjective sensation of seeing a luminous star and a track between P and P'.

The appearance of tracks might indicate the existence of "streaks" or tracks within the retina, with the older part of the track becoming fainter as it becomes extinct. It is also possible that the tails are optical illusions, the results of an unsuccessful effort to focus the eyes on the origin of the light (Fig. 3).

The minute ionizing core of heavy nuclei represents an energy exchange corresponding to a dose of more than 10^8 rads within a few ångströms of the core. If the passage of such particles causes irreversible deterioration of retinal cells and of neurones, then in a long space flight outside the Earth's magnetosphere, a significant degree of random cellular damage might result.

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Preliminary Observations on Tickling Oneself

WHY is it that most people cannot tickle themselves? Darwin observed that "from the fact that a child can hardly tickle itself, or in a much less degree than when tickled by another person, it seems that the precise point to be touched must not be known"¹. (There may be differences between man and other primates. The Kelloggs observed that their chimpanzee Gua was "frequently observed in the process of tickling herself and laughing as a result"².) But this hypothesis seems *prima facie* incorrect, or at least inadequate, as most children can be tickled even when they know where and when the tickle stimulus is to be applied. No experimental work appears to have been reported on this question, and Darwin's interest was primarily centred on the biological value of ticklishness and laughter. The problem is perhaps not trivial; evidently knowledge of some sort is necessary for the cancellation of the ticklish sensation, and it has been shown that cancellation of other signals (for example, those that arise from voluntary movement of the eyes) seems to be produced by self-generated "command" signals rather than by external feed-back^{3,4}. Does a similar mechanism exist for the tactile system? Another question is whether pain is subject to the same type of control; if so, there could be practical clinical applications.

For this experiment we constructed an apparatus that allowed a comparison to be made between self-administered and externally administered stimulation. The apparatus also allowed the stimulus to be accompanied by passive arm movements in phase with the movement of the stimulus when it was externally controlled. We could assess, therefore, whether external feed-back to the skin and muscles associated with the movement was important in providing cancellation signals.

The apparatus (Fig. 1) provided a standard stimulus consisting of a plastic pointer moving on the sole of the bare foot. A box was constructed with a slot in the upper surface, over which the bare foot was placed. A pointer (F) projected through the slot and was counterweighted (E) to maintain a constant pressure while traversing the length of the slot. The pivoted pointer plus weight could be moved along slots in the side of the box (H) by means of the attached handle (D). Movements were synchronized with the beat of a metronome. The diameter of the pointer tip was 1 mm, applied with an upward pressure of approximately 17 g. The movement was limited to 10 cm and took place once per second for 4 s.

Thirty undergraduates were tickled in two out of three conditions: active E (in which the experimenter tickled the subject, S, with sole control over the handle); active S (in which the subject tickled himself, with control over the handle); passive (in which the experimenter controlled the handle, but S held it and his arm passively followed the movements). Subjects were divided into three groups and each group made a comparison of two conditions. Each subject was given four trials, on each of which the two conditions were presented successively on the same foot for four seconds each. Alternate feet were used on each trial and the order of presentation was changed on the second and fourth trials. After each trial the subject was asked if the conditions differed in ticklishness and invited to make further comments. A unit score was assigned for each subject on each trial in which one condition was rated as more ticklish. A difference score could thus be computed

for each subject over the four trials, indicating the strength of a tendency to rate one condition as more ticklish than another.

All subjects in the relevant group (there were ten) stated that being tickled by the experimenter (active E) was more ticklish than tickling themselves (active S), and the difference score is highly significant (*t* test) ($P < 0.001$). Being tickled by the experimenter (active E) was also judged more ticklish than the passive condition by all but one subject (out of nine), who found the conditions equally ticklish (difference score, $P < 0.001$). Finally, the passive condition was more ticklish for eight (out of eleven) subjects than tickling themselves (active S), and in only one subject was the opposite found (difference score, $P < 0.05$). Most subjects (77%) also commented that the tickle became less strong as trials proceeded.

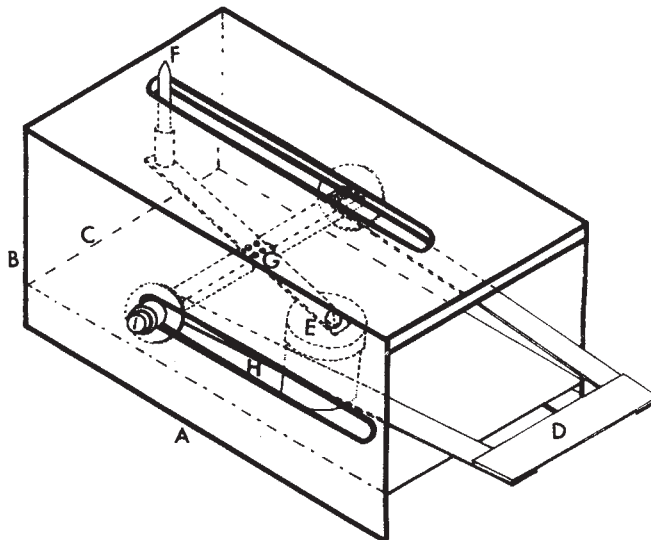


Fig. 1 The tickle apparatus is shown here (see text for explanation).

Thus, there was no difficulty in confirming experimentally that a self-administered tickle is less effective than an externally administered tickle. But we must consider the implication of the finding that passive arm movements reduced tickle strength, but not to the level of self-administered tickle. We administered, in all three conditions, the same stimulus to the sole of the foot, and therefore the difference in response must be attributed to the mode of delivery. A self-administered tickle is delivered with two types of knowledge—first, the "command" that results in the actual delivery of the tickle stimulus, and secondly, the feed-back stimulation produced by arm movement during the delivery of the stimulus. An externally administered tickle has neither. The passive arm movement condition eliminates the command signal but retains the feed-back information. Therefore, the most parsimonious interpretation of these results is that the cancellation signal is not entirely based on the command signal—were that the case, both a self-administered tickle and the passive arm movement condition would be the same. It is possible, however, that the passive condition did not represent true passivity, and that the subjects were clandestinely assisting or resisting the progress of the pointer in this condition, and that the three conditions varied in subtle respects in allowing the subjects to predict the fine timing of the stimulus delivery, in spite of the metronome beat, and that such a precise prediction is critical. Both possibilities could be explored further experimentally by arranging that the stimulus be delivered automatically, but under varying degrees of remote control by the subject, and with varying degrees of phase lag. If such an arrangement succeeds in reducing or eliminating the

tickle, the question of prediction versus command signal could be examined by eliminating the control by the subject but providing detailed information on the position and velocity of the stimulus.

It is possible that pain or other sensations would show a similar difference between self and externally administered stimulation. Stengel⁵ found that among certain patients prone to inflict severe self-mutilation there was no corresponding insensitivity to externally inflicted pain. The methods used here indicate that the topic is not intractable to experimental treatment, although we have not achieved a final answer.

The experimental work was carried out in the Psychological Laboratory, University of Cambridge.

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Floating Vegetation of Lake Kainji, Nigeria

FEARS¹ that Lake Kainji in Nigeria would become infested with the water weed *Pistia stratiotes* have not been borne out by recent events. This man-made lake now seems to be free of weed, in contrast to similar lakes elsewhere. At Kariba (area 4,300 km², closed in 1958) where the lake took 4.5 yr to fill, extensive mats of *Salvinia auriculata* and *Pistia stratiotes* accumulated over much of the lake, covering over 10% of the surface by 1960 and more than 22% by 1962 (refs. 2, 3).

Water hyacinth, *Eichornia crassipes*, and the water fern *Ceratopteris thalictroides* invaded large parts of Lake Brokopondo in South America (area 1,500 km², closed in 1964) during the first 2 yr⁴. Lake Apanas in Nicaragua and Lake Rio Lompa in El-Salvador were similarly infested by the water hyacinth during the early years of filling⁵. In Lake Volta in Ghana (area 8,500 km², closed in 1964) *Pistia stratiotes* was the nuisance weed.

In Lake Kainji in Nigeria (area 1,250 km², closed in August 1968) three main types of floating plants have been recorded. These are algae, *Pistia stratiotes*, and a grass, *Echinochloa pyramidalis*. The growth of algae has been most prominent of the three. During the first 18 months, several algal surface blooms formed by *Anabaena*, *Microcystis*, *Volvox* and *Eudorina* spp. were recorded. These luxuriant algal growths provided food for herbivorous fishes such as *Distichodus rostratus*, *Citharinus citharus*, *Alestes baremose*, *Synodontis membrana-*

nous, *Labeo coubie* and *Labeo senegalensis*, and seem to have made up for the small development of an "aufwuchs" (attached algae and other plants with associated animals) which would otherwise have been the main diet of these fishes. Small quantities of submerged plants *Utricularia inflexa* and *Ceratophyllum demersum* were also found but these formed a very minor part of the aquatic vegetation.

Pistia stratiotes and *Echinochloa pyramidalis* invaded only small parts of the lake margins during the first year (less than 0.5% of the lake bottom). *Pistia* was found mainly during the dry season and has since receded progressively. By June 1970, not a single plant was found in the lake. *Echinochloa* formed small islands which were either rooted near the edge (in water even as deep as 6 m) or floating. In the former case the plants had long stems which kept the leaves above water while, in the latter case, the stems were only 1–1.5 m long. As with *Pistia*, floating islands of this plant had disappeared by July 1970. Thus in the first 2 yr after the Kainji dam was closed the lake has not developed a weed problem.

The question is: will there be a weed problem in the future now that the lake has developed beyond the early filling phase when plant and animal invasions and population explosions are known to occur⁶?

What factors have retarded the growth of vascular aquatic weeds at Kainji? The two notorious weed species *Salvinia auriculata* and *Echiornia crassipes* do not exist in the Kainji area of Nigeria⁷. *Salvinia nymphaeella*, which is found at Kainji, is native to West Africa and has not been reported to form mats anywhere. Furthermore, it is now recognized that *Pistia* and indeed any other potential weed could not form extensive mats at Kainji for two main reasons. First, 70% of lake surface was cleared of vegetation and burnt before impoundment, which not only reduced the initial nutrient enrichment of the water but also retarded the growth of plants which would otherwise have been rapid within the quiet and stagnant water between trees standing in the lake⁸. Frequent and regular winds also tended to destroy any mats which had formed.

But by far the most important reason is the hydrology of the lake. The ratio of outflow to volume of the lake is 4.1 (ref. 9). Its mean retention time (capacity/inflow) has been calculated as 76 days¹⁰. This means that the whole lake water is changed about four times per year. This creates a rather large (10 m) and rapid fluctuation in lake level (or drawdown) and a large seasonally exposed shore line where littoral flora are stranded and killed. A similar effect of water level on aquatic weeds was recorded in Kariba in 1964 where a rapid and drastic drop in water level caused a 4% decrease in the area covered by *Salvinia*¹¹.

It must be pointed out that such losses of littoral flora are likely to affect the productivity of fish through the destruction of spawning grounds and the removal of both the protection enjoyed by juvenile fish and the substrates for the growth of "aufwuchs" algae. Nevertheless, it now appears possible that a combination of fortunate circumstances has produced a weed-free man-made lake in Nigeria. How long this lucky situation will last remains to be seen.

We thank the Rockefeller Foundation and the US National Academy of Science for their support in this and other surveys in the Kainji lake area.

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Generalizing and Abstracting

IN theories and experiments on concept formation, the terms generalization and abstraction are often used in an equivocal sense, frequently as synonyms to describe the process of forming a concept from perceptual or verbal data. In one sense, however, the terms are distinct, as for example, when a concept name shifts its meaning from the concrete-general to the abstract-particular, as in the following sentences involving the concept "ballad". (1) A ballad is a piece of creative writing. (2) The ballad is a literary form. We can describe any concept by a double notation, made up of (i) $a_0, a_1, a_2 \dots$ levels of abstraction, where a_0 is the concrete, and (ii) $g_0, g_1, g_{11}, g_{111} \dots$ degrees of generalization, where g_0 is the unique or the particular.

In the first sentence the term ballad is used in the concrete-general sense (a_0g_1) although in the second sentence it is used in the abstract-particular sense (a_1g_0). The word ballad is thus a homonym in which there is an intimate relationship between its two meanings.

One way of defining the act of abstracting would be as the shift in meaning from the concrete-general to the abstract-particular, as for example ($a_0g_1 \rightarrow a_1g_0$). Such a shift of meaning is frequently demanded in higher level writing and thinking and the frequency of its usage might indicate advanced cognitive ability.

Table 1 Frequencies of Response

Group	n	Abstract- ing	General- izing	Others	Total
Newly graduated students	66	607	834	539	1,980
First year students	22	149	275	236	660
Fifth year sec. school	70	389	712	999	2,100
Third year sec. school	66	221	623	1,136	1,980
First year sec. school	63	138	561	1,191	1,890

n, Number of people involved.

A psychological test of such a shift can be constructed which makes use of the double meaning of such concept words as ballad, by leading the thinker from the concrete-particular to the concrete-general, and then to ask for a response at a third level, it being assumed that a concrete-general is formed before an abstract-particular. This third level can be tested by a multiple-choice form, incorporating possible responses which individually involve generalization and abstraction, as well as illogical but meaningful alternatives incorporating synonyms, constituent parts and partial associations.

Here is an example. The subject is asked to underline the word or phrase in the column on the right which he thinks most appropriately completes the row of three terms.

The worm dangling at the end of my fork	invertebrate	(1) useful garden creature
		(2) living organism
		(3) earth dweller
		(4) zoological grouping
		(5) snail

In terms of the notation used we have:

particular worm	invertebrate	living organism
a_0g_0	$a_0g_1 \rightarrow$	a_0g_{11}
	invertebrate	zoological group
	$a_1g_0 \rightarrow$	a_1g_1

If the person tested underlines "living organism", it is assumed he is thinking of invertebrate in the concrete-general sense, but if he chooses "zoological grouping", it is assumed he is using invertebrate in the abstract-particular. The occurrence of other choices gives an indication of illogical connexions.

A test of thirty such items was given to a group of newly graduated students, newly entered first year undergraduates, and fifth, third and first year secondary school pupils. The results are given in Tables 1 and Table 2 (in which the frequencies in 1 are converted to percentages).

Table 2 Percentage Responses

Group	n	Abstract- ing	General- izing	Others	Total
Chance		20	20	60	100
Newly graduated students	66	30.7	42.1	27.2	100.0
First year students	22	22.6	41.7	35.7	100.0
Fifth year sec. school	70	18.5	33.9	47.6	100.0
Third year sec. school	66	11.1	31.5	57.4	100.0
First year sec. school	63	7.3	29.7	63.0	100.0

From the percentages (Table 2) it is clear that the capacity to make abstractions in the sense defined here increases steadily through adolescence and into adulthood. The increase in the ability to generalize is less marked. The results seem to confirm that persons involved in higher level learning, such as is carried out at university, develop this capacity to use the abstract-particular form of concepts. Among the graduates, the English honours students made a marginally larger number of abstracting responses. It should be noted that all the secondary school groups made fewer abstracting responses than would be expected by chance.

This method of measuring the capacity to abstract could lead to interesting studies of different groups of adolescents and young adults in different educational and sociological settings.

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BOOK REVIEWS

Running Out of Space

The Making of an Ex-Astronaut. By Brian O'Leary. Pp. xii+243+10 photographs. (Michael Joseph: London, April 1971.) £2.25.

How would you feel if, on turning up for a new job, you were told "We don't need you around here, at least not for the time being"? This was the welcome accorded Brian O'Leary and ten other would-be scientist astronauts when they reported for duty at Houston in September 1967. If it hadn't been for the gruelling effort needed to get the job—described by O'Leary in detail and with humour—and its miserably poor salary, you might expect at least a few of the XS11 (excess eleven) to give up on the spot. Nobody did, until Brian O'Leary quit just seven months later.

O'Leary gives two reasons for his departure. One is the tale of Dr Brian T. O'Leary, scientist and ex-astronaut (well, almost); and the other is of NASA's scientific programme.

As a person O'Leary is far from unique. He was just a bright youngster who was awed by space. When he was a youngster there was little chance of going into space, so he became an astronomer instead. "At Berkeley I became a professionally recognized planetary astronomer, a space-age breed who snoops around the solar system with unmanned probes and Earth-bound telescopes."

While O'Leary's humour keeps the book readable, *The Making of an Ex-Astronaut* gets more interesting when O'Leary arrives at Houston, an ecological disaster area if ever there was one. The astronauts live a remarkably dull life and, if O'Leary is to be believed, most of them are quite dull people. "There they were in sport shirts and crew cuts—the military pilots, only children, eldest children, mid-westerners, worshippers, Boy Scout leaders, hunters, aerophiles, and sports car racers." It may be this that has kept them out of the autobiography stakes rather than the restrictive Time-Life contract "which provides \$200,000 cash each year to be shared equally among astronauts and astronauts' wives in exchange for the sole rights to astronauts' stories".

The book really begins to hit home when O'Leary lays into NASA's cavalier attitude to science—the misorganization of the science programme and NASA's insistence that astronauts undertake a year's training to become high performance jet pilots finally drove O'Leary to resign. This disregard of science and the astronaut scientists is baffling. The first lunar landing may be justified on

purely exploratory grounds, but "how long will the public buy operational lunar landings performed solely by test pilots at a billion dollars a shot?"

O'Leary cites examples of "a test pilot's shortcomings as a scientific observer on Apollo", and comes to the conclusion that "Now is the time to start including a scientist on an Apollo crew". But scientist astronauts with excellent qualifications are grounded "while rookie pilot-astronauts plan to explore the lunar surface".

Science could help rescue the Apollo programme from its lack of direction. Without some sort of rethink the resignations—O'Leary was the first of several scientist astronauts and scientists—will continue. "The scientific reasons for space exploration are to me the most compelling. To answer such questions as, what are the Moon and planets like? Where did we come from and how did we evolve? How does man react to prolonged weightlessness? What is the universe like, now that we can see it through space rather than through our murky atmosphere?"

Despite NASA's foolish disregard of science, O'Leary manages to throw aside his pessimism and turn his starry eye to the possibilities of the space effort. O'Leary is not a brilliant writer, but he is amusing and his subject is inherently interesting to any scientist.

MICHAEL KENWARD

Earth in the Open

Understanding the Earth: A Reader in the Earth Sciences. Edited by I. G. Gass, Peter J. Smith and R. C. L. Wilson. Pp. 355. (Published for the Open University by Artemis: Horsham, Sussex, 1971.) £3.50 boards; £2.10 paper.

THIS book is a compilation of mostly original articles under the editorship of staff of the Department of Earth Sciences at the Open University. It has been produced in the remarkably short time of nine months in order to provide an up to date and well informed synopsis of particular facets of Earth science at a level suitable for first year university and school courses. There can be no question that the editors have largely when the book is considered in its largely fulfilled their objectives, particularly principal function as a reader within the Science Foundation Course of the Open University, where it forms the link between chemical/biological sciences and studies of the atomic basis of matter. This assured market has also allowed the book to be published at a remarkably low price.

It opens with chapters on mineralogy—petrology and radioactive isotope dating methods, and then turns to consideration of the Earth as a planet; its magnetic field, internal temperatures, the Chandler wobble and comparisons with the Moon. A chapter on meteorites precedes three chapters devoted to the origin of life and the Earth's atmosphere, and a further three on the evolution of life and geomorphological surface features of the Earth. Seven chapters are then devoted to the chief concepts of continental drift and plate tectonics and their relationship to mountain building and volcanism, with asides on possible significances of reversals of the Earth's magnetic field. The relevance of these geotectonic studies to Man is considered in the final four chapters dealing with the location of African ore deposits, the detection, prediction and control of earthquakes and nuclear explosions, and finally the political background of the ill-fated Mohole project.

The content is deliberately unbalanced, giving weight to those areas which the editors consider to be growth points. This results in the excessive compression of mineralogy and petrology into one chapter, and palaeogeography, geomorphology and stratigraphy into another. These are done remarkably well in the space available, although a fuller treatment would have been preferable and space made available by reducing the three chapters on the origin of life, atmosphere and the primitive Earth to a single chapter, particularly as all three are in fact largely concerned with the origin of oxygen in the Earth's atmosphere. Furthermore, whole chapters on the Chandler wobble and the oxidation: polarity paradox could well have been relegated to sections of existing chapters, thus providing space for either the expansion of more basic geological concepts, such as geosynclines, or at least one or two other growth points—the evolution of the Earth's crust, the time of separation of the core, the origin of greenstones, the significance of gravity anomalies, the thermal history of a convecting Earth, and so on—which are almost entirely ignored. It might, however, be even more fitting for the reader to include further items of direct human interest such as the problems of the origin and distribution of oil and natural gas or other biological/climatic deposits. My chief criticism of the choice of topics, however, is the example of geopolitics, the Mohole project, which, although having the elements of farce, was not a fiasco as it gave rise to the JOIDES deep-sea

drilling programme. Surely a more relevant political and human slant would have been obtained by describing the attempts and necessity for international agreements on the exploitation and pollution of the ocean floors?

These objections, however, to detailed choice of topics are, of course, somewhat subjective and, with so many problems awaiting study, the editors could have only slightly increased their coverage. The general content of the book is, in fact, very good. Clearly more time could have reduced some of the repetition, although this is not serious, but I feel the index has suffered greatly from the speed of production, being incomplete both in subject matter and the page references given. Unfortunately it was also the editorial policy that there should be no references and only a few bibliographical references are given for each chapter—never more than six and sometimes none at all. As a result the reader is, for example, only recommended in chapter 21 to a small part of Arthur Holmes's *Principles of Physical Geology* and it is not recommended for the physical geology chapter. It is understandable that the editors should think that their readers would be put off by a long bibliography, but that should not have prevented a supplementary list of either specific references from the text, or of other works to which the real enthusiast could turn.

In short, it is a very good book indeed—but it could have been excellent if just a little extra thought had gone into the original plan and an extra month into the final editing and referencing. D. H. TARLING

Further Education

The Extra Year: The Raising of the School Leaving Age. Edited by J. W. Tibble. Pp. 134. (Routledge and Kegan Paul: London, November 1970.) £1.75.

As the raising of the school leaving age approaches, yet again, a lot of worried people will be wondering what to make of the extra year. This book is intended to help them; and parts of it will. But why do educationalists relapse so easily into cant? Anyone who is shocked at the barbarity of the educational right wing should read this sort of book: it will help him to understand the tone of bloody-minded exasperation that characterizes Black Papers and *Daily Telegraph* leaders.

Take a few examples. Albert Rowe, clearly a perfectly sensible headmaster in real life, urges us to "recognize that all cultures are relative and have validity" (Alf Garnett's, for instance?) and concludes that "the phrase 'higher cultural standards' is . . . as it stands,

meaningless". Tyrrell Burgess calls for a nationwide system of "vocationally relevant" Colleges of Further Education, taking all kinds of pupils from the age of fourteen or fifteen onwards and teaching them all "a common core of subjects . . . (that) would include maths, English, science, psychology, sociology and economics". (Odd how these books tend to start with appeals for more science and technology and end by offering more social science.) "And one wonders," he says, "if it could be anything but beneficial for full-timers and part-timers to find themselves in the same classes for these common-core subjects." (Well, yes—one does.)

J. D. McAulay, an American professor of education, says "such courses as English, history, science, foreign language and mathematics, which many (mistakenly) believe are in themselves educative . . . become the rocks upon which many a youth is broken. Such youth need different facilitating experiences, those which will give them courage to face and solve unique dilemmas, to be conscious of the needs of others and to establish one's self-integrity" (and one's grammar?). He reports with enthusiasm that "The Chief of Police of the City of Chicago" wants "a completely professionalized force" recruiting "a complete man who has . . . a sense of perspective that can only come from a knowledge of history and philosophy." (Did Mayor Daley agree?) In short, this book is full of wind.

But some of it is well worth reading. John Sheehan, in a wholly cant-free chapter, argues that the economic advantages of raising the school leaving age are exceedingly uncertain, while the economic savings alleged to justify its recurring postponement are trivial. The decision should therefore be a social and political one. Denis Lawton shows how important a force the Schools Council, local Teachers' Centres and various curriculum development projects are becoming, and tells us which of their reports to read. Colleges of Further Education must indeed become an increasingly central part of our educational system, and Tyrrell Burgess is quite right to explain why.

Other contributors—Professor Tibble, Malcolm Seaborne, S. F. Eggleston and Albert Rowe—give us a useful summary of progressive wisdom about upper secondary education, its past, present and future, and Professor McAulay tells us interesting things about the history of the American high schools. Their chief message is that raising the school leaving age will make it clearer than ever that schools can only work with the willing consent of their pupils—something teachers may win but cannot command.

DAVID DONNISON

Research by Experiment

Investigation by Experiment. By O. V. S. Heath. (The Institute of Biology's Studies in Biology, No. 23.) Pp. 74. (Arnold: London, November 1970.) £1.00 boards; £0.60 paper.

MANY courses are given to aspiring scientists as introductory statistics or biometrics introducing elementary statistical methodology. The objective, however, is not to help budding statisticians to statistize but to help experimental scientists to experiment properly. That statistical techniques will help cannot be seriously disputed, but the chief objective of such courses should be to make students think in a logical fashion about their experimental situations. A feature of the teaching of the present courses seems to be that students learn to substitute for logical thought improperly understood statistical techniques. Some of the blame must fall on the statisticians who give these courses when they become absorbed in the techniques at the expense of expounding the underlying principles. Such courses should be in formalized common sense based on an elementary study of probability and the normal distribution.

Professor Heath's little book (it is not as small as the 65 pages of text might suggest, for the print is rather small) sets about this task in an easily comprehensible way for students. The first chapter of the three into which the book is divided is particularly good on this account. He makes the point that the scientist, unlike the mathematician, cannot prove. He can only disprove. An established theory only holds until evidence is produced to disprove it, and the timing of such an event cannot be predicted. Students and research workers who realize that they should set about disproving their hypotheses seldom design poor experiments. Those who imagine that they can prove their hypotheses tend to overlook even the most rudimentary precautions.

I have three minor criticisms. On page 28 it is stated "The only way to obtain a representative sample from a population is to take a *random sample*. . . ." If a representative sample is defined as a random sample, well and good. A wiser course would have been to concentrate on the unbiased properties of the random sample in estimating population parameters, pointing out that these make it the most desirable type of sample. On pages 51 and 52 there is a short discussion on the disadvantages of systematic designs for scientific research. The argument gets sidetracked in detail. The fundamental objection is that scientific research attempts to produce unbiased estimates of population parameters with a

measure of their fallibility depending on the mathematics of probability and randomness. Logically the mathematics of the probability for systematic designs cannot exist and hence systematic designs should not be used.

In these days of decimalization and metrication it is a pity that SI units were not used as this will date a very useful little book prematurely. I have, however, no hesitation in recommending it as reading for A-level, undergraduate science students, and those wishing a simple exposition on the philosophy of experimentation.

A. A. RUTHERFORD

Tumour and the Virus

Viruses and Cancer. By Sir Christopher Andrewes. Pp. 166+24 plates. (Weidenfeld and Nicolson: London, November 1970.) £2.75.

SIR CHRISTOPHER ANDREWES has written a welcome summary of the chief trends in virus research in relation to cancer. His new book contains no unjustified inferences and no pretentious speculation. Dr Andrewes stays close to the facts with admirably good judgment and a historical perspective which is both perceptive and well balanced. The book sweeps across the diverse phenomenology of virus-induced tumours occurring in nature or under laboratory conditions. The inherent problems in research on human cancer are clearly brought out. The importance of conditioning factors in the development of cancer is adequately emphasized.

Andrewes's book begins with a definition of virus-induced overgrowth and cancer, and a brief review of the viruses involved. He points out that, just as tumours which have been transplanted in series are very different from spontaneous ones, so also are serially propagated oncogenic viruses different from their "wild" progenitors, a fact not widely enough appreciated. Andrewes emphasizes the growing belief that the appearance of a clinically recognizable neoplasm is evidence that the defences of the host have been overrun. His survey of tumorigenic viruses offers no clues as to what fundamental properties may be a necessary prerequisite of tumorigenic potential in viruses or which viral genes may be directly involved in neoplastic transformation.

A series of chapters is devoted to tumours induced by RNA containing viruses. A historian's delight is Andrewes's reference to the views of J. B. Murphy, who emphasized in 1931 that the chicken sarcoma agent behaved as a "transmissible mutagen" and likened its action to that of the trans-

forming principle in bacteria. The complexities of the virus-host relationship are well brought out in the extensive discussions of fowl tumours and leukaemias, breast cancer in mice, and leukaemia in numerous mammals. It is, however, unfortunate that the results of recent work on the host range of different strains of Rous sarcoma virus have not been utilized to place the helper virus phenomenon in its proper perspective.

In opening a discussion of DNA containing tumour viruses, Andrewes points out that infectious virus may disappear from the tumours caused, even though something of the virus remains, perhaps closely integrated with the cell. Andrewes gives due credit to R. E. Shope for recognizing, in rabbit papilloma, that virus may exist in the warts in an incomplete or masked form. Shope later suggested that the virus might be there as DNA. Dr Andrewes makes clear that it was the work with cloned populations of polyoma virus which got across in a forceful way the concept that a single virus can cause a variety of different types of tumours depending on the cell type which it infects. Similar conclusions can also be drawn from the study of the pathogenic potentialities of individual RNA containing fowl tumour viruses. There is an up to date discussion of the properties of virus-transformed cells, including the appearance of new tumour antigens. The coverage of tumours associated with DNA containing viruses extends from those in frogs and fishes to malignant lymphoma in children and cervical carcinoma in women. Evidence of a causal relationship between the virus and tumour is available in some of these tumours, but not in others. There is always the problem of a virus found in a tumour being a mere passenger; this applies both to DNA and RNA containing viruses. There can be no doubt, however, as Andrewes points out, that in nature there exist a variety of viruses with tumorigenic potential.

There is a thoughtful chapter on experiments on synergism. The failure of cytotoxic viruses to serve as useful oncolytic agents is well documented. The author brings to focus the developing field of tumour immunity, placing particular emphasis on cell-mediated defence mechanisms. The book concludes with a chapter on unanswered questions. Andrewes points out that some forms of leukaemia in man are so like those of other species that a viral cause seems by analogy highly probable. To obtain evidence has so far proved to be a very difficult task. New techniques, however, are being invented or perfected. Andrewes notes that if human cancer viruses do exist they are likely to be widely occurring

agents. Their ability to lead to development of cancer would probably depend on a variety of factors, not merely the presence of the virus.

This book is necessarily diverse in content. Any book on viruses and cancer which attempts to describe the phenomena comprehensively would make for somewhat uneven reading; Andrewes's style, however, is succinct and clear. His book should be useful to anyone wishing to obtain an objective overview of this complex but important field.

IGOR TAMM

Enzyme Reactions

Enzyme-Catalysed Reactions. By C. J. Gray. Pp. xiv+364. (Van Nostrand Reinhold: London and New York, February 1971.) £7.50.

THE author of this book describes his aim when he writes: "Although the field is too large for this book to include a discussion of every enzyme, I have tended towards the more comprehensive, and I hope more objective, approach in that a relatively large number of enzymes have been discussed individually. This allows the reader to see for himself as broad a picture as possible of the whole field." It is difficult to fulfil this aim in 350 pages, but a good attempt has been made to give honours students a purely descriptive text on as wide a range of enzyme reactions as they need to know about. The book will certainly help students to pass examinations if they have a reasonable memory, but there should be more to a book than a mere recital of facts. Surely every author hopes that he will excite the interest of at least some of his readers. I am very doubtful whether anybody reading this text will be inspired with the burning desire to study enzymes from a physical, chemical or biological point of view.

In the first 90 pages, the physical background to enzyme catalysis is treated at a level which is totally inadequate for a modern course. This space could well have been used to increase the conceptual material in the subsequent chapters on different types of enzyme reactions. For instance, it is my experience that students like to see, even during a theoretical discussion, some examples of how the facts have been obtained. Some well chosen experimental demonstration would have increased the general appeal of the text.

Dr Gray has done an enormous amount of work and he has been successful in producing a book which will be useful to undergraduates. My criticisms are not directed towards him, but towards the publishers. In my opinion the publishers have failed this author in two respects. First, the refereeing and editing of this book were

totally inadequate. While I am all in favour of publishers supporting young authors rather than running after the big names, reviewing by experienced people is essential to avoid some of the mistakes made in this book. Second, I regard the quality of the production as very near scandalous. If one buys a textbook of 350 pages for £7.50, one does not expect to find such a low standard of printing.

H. GUTFREUND

Elements of Fluidics

A Guide to Fluidics. Edited by Arthur Conway. Pp. 146. (Macdonald: London; Elsevier: New York, March 1971.) £2.50.

THE first dynamic fluidic elements were announced a little over ten years ago by the Harry Diamond laboratories, Washington, but if the extensive bibliography at the end of this book is anything to go by, almost no books—as distinct from papers and conference proceedings—seem to have been published on the subject. This book would therefore appear to be timely, although it is much more difficult to assess its quality than that of a solid state physics or electronics text, for example, which can be compared with a countless number of similar books—some good, some very bad—all of which claim to be the last word in lucid communication.

Contributors to the eight independent chapters of *A Guide to Fluidics*—of fluidics in particular industries and fields of endeavour—are an interesting mixture of industrialists and academics. The opening chapter on the fundamentals of the subject would certainly give adequate and self-sufficient information to any reader who wants to know what fluidics is all about—the basic physics of most devices, the various types of amplifier and the logic operations which can be performed. The intelligent layman should not fail to grasp the gist, if not the finer detail, of what is described.

One of the boasts of the advocates of fluidic elements is that they are more dependable than electronic components and can operate under much more adverse conditions. It is therefore inevitable that the medical profession should have taken advantage of this new technology to provide reliable control circuits for heart pumps, lung ventilators and an ingenious self-cleaning filter circuit for an artificial kidney system. All are described in the chapter on medical applications.

Halfway through the book, the reasons why the rapid development of fluidics in the early 1960s has tended to fall off recently become clear. It certainly seems that the development of interface devices—to translate the

signals from fluidic elements dependably into controlling actions—has lagged behind, and the whole technology must mark time while it catches up.

The extreme conditions encountered by monitoring devices in nuclear reactors rule out most conventional electronics, except, perhaps, for thermocouples, and indeed fluidics have turned out to be extremely valuable for examining, for example, the state of coolant. A particularly interesting marine application for fluidics is a bow thruster for ships manoeuvring in confined spaces; a large wall-attachment amplifier can be used for this purpose. Aerospace applications include guidance systems for missiles and conventional aircraft alike.

The concluding chapter on trends and prospects succinctly sums up the state of the art by saying that “fluidics is just beginning to be taken seriously”. This book has doubtless made a successful attempt to help it on its way.

ROGER WOODHAM

Infrared Analysis

IR Theory and Practice of Infrared Spectroscopy. By Nelson L. Alpert, William E. Keiser and Herman A. Szymanski. Second edition. Pp. xiv + 379. (Plenum: New York; distributed in Europe by Heyden: London, December 1970.) £8.80.

THOSE who are familiar with the first edition of this book will note, probably first, that the second edition is almost twice the price, but that it has gained an additional author as well as some rewritten and some entirely new material. By dint of squeezing the type slightly, the publishers have kept the length of the second edition to within a few pages of the first.

Chapters 2, 4 and 5, which together constitute some three-quarters of the book, are virtually unchanged. Some figures have been added to chapter 2 (on instruments) to illustrate the effect of changing scan speed and resolving power on a recorded spectrum, and some formulae relating various operating parameters have been included, which will be useful to the beginner when operating an infrared instrument. With the exception of a very brief nod in the direction of computer assistance, the remainder of the chapter is unchanged.

The body of the text of chapter 4 (“Theoretical Considerations”) is quite unaltered; this is good, for I heartily recommend Professor Szymanski’s approach, with his clear discussion of group theory and the concomitant behaviour of fundamental, overtone and combination vibrations of a wide

range of molecules. I note, however, that an error in the first edition in Fig. 4.30 has been carried into the second; the long and short arrows on the diagram illustrating the Coriolis forces on the ν_2 vibration should be interchanged. In fact the only change in this chapter has been a slight extension to the final list of references.

Similarly, chapter 5 is identical in both editions, except for the addition of an eight-page section outlining a logical method for analysing an unknown infrared spectrum; this also offers some twenty practice spectra (for the strong-minded only, for a discussion of each spectrum is given in the text). In almost every one of these examples—as in real life—a complete analysis is not possible from the infrared spectrum alone, and it is a pity that the necessity for using supporting data from other techniques is not made clearer in the text—the logical gap between, for example, recognizing a spectrum as that of a primary alcohol, and the bald statement that the substance is n-butyl alcohol, will be very disconcerting to the beginner.

The original chapter 3 (“Laboratory Techniques and Preparation of Samples”) has been replaced by a useful general chapter on accessories, which includes mention of polarizers and ATR units, as well as a description of the more common gas and liquid cells. Much of the material from the original chapter 3 has been moved, with additions, to a new chapter 7, “Sample Handling Techniques”, where we learn about infrared solvents, mulling and pelleting techniques and so on. The large spatial separation between chapters 3 and 7 in this edition is somewhat misleading, for some of their material is common, although covered from slightly different viewpoints.

The twenty pages of chapter 6, “Quantitative Analysis”, represent the real difference between the two editions. The chapter has been entirely rewritten and, though somewhat shorter than before, contains sufficient information for an unskilled operator to tackle quantitative work in a useful and logical way. And finally chapter 8, outlining a spectra reference library, has been updated in a token fashion by the inclusion of three or four books published since 1964. The discussion of DMS and similar spectral card series is useful, but it is now many years since the DMS literature card system was discontinued in favour of a literature list indexed by IBM punched cards.

In summary, this book is still a very valuable and worthwhile addition to the infrared library; whether or not possessors of the first edition will, or should, flock to bring their library up to date with the second is another question.

C. N. BANWELL

CORRESPONDENCE

More Means Worse

SIR,—In your issue of January 15¹, your staff open their report of the Cambridge education conference by saying that everybody at it rejects the Amis view that “more means worse”. That is a vulgar misquotation which perhaps recommends itself to educational expansionists by being easy to dismiss as “narrow”, “facile”, and so on.

What I wrote (in 1960), displaying no more than ordinary powers of prophecy, was “more will mean worse”; this in the context of arguing that, if you stop caring about university admission standards and allow simple desire for higher education to be the chief passport to it, you will produce less well educated graduates. Those who, like your staff and/or the participants at the conference, plus lower forms of life like the education correspondent of *The Times*, don't know what I said about more and worse, clearly can't know my arguments for saying it, and are in no position to “reject” a “view” I have never stated or held.

I would not, of course, use the same phrase today. Overcoming my dislike of stating what is perfectly obvious and more and more widely accepted (outside places like your columns and education conferences), I should have to write, “More has meant worse”.

Yours faithfully,

KINGSLEY AMIS

*Lemmons,
Hadley Common,
Barnet, Hertfordshire*

¹ *Nature*, 229, 159 (1971).

Careers in Government R & D

SIR,—I am afraid that your editorial (*Nature*, 230, 334; 1971) misunderstood the basis of the CBI's proposals for broadening career prospects for people entering government research and development. The purpose of the short-term appointment was to offer the opportunity for a few years government service as an alternative to entering government science as a life's career. Incidentally, initial reactions from government suggest that their thinking is on broadly similar lines, so I hope that CBI will still have some friends in government laboratories!

As for the rest of your comments, the CBI's proposals called for just the same opportunities for lateral movements with-

in government service as your own commentary suggested and we explained how this might be achieved.

You will be interested to hear that we have other papers on various aspects of government and its research and development in preparation. We felt the paper on careers to be the most important since a flexible career-structure will make it easier for government to introduce any future changes in emphasis of government research and development.

Yours faithfully,

P. M. KNOWLSON

*Confederation of British Industry,
21 Tothill Street,
London SW1*

Uses of Education

SIR,—I should like to comment on Sir Eric Ashby's analysis of what is wrong with university education today (*Nature*, 230, 283; 1971), because I believe that in supporting the remedies proposed by Pippard *et al.* he fails to grasp the nettle.

Universities may well stand for excellence, objectivity, the cultivation of reason and the inherent value of knowledge, but unfortunately so many people, parents, employers and government departments believe that they stand principally as professional qualifying bodies. The former of these roles is much the more important, yet it is hardly for such purposes that universities have multiplied and grown in size over the past decade. Let us be clear that the reason most students compete for university entrance is not the altruistic one of promoting excellence and so on but to acquire a qualification which has high market value. Would it not be better to recognize frankly that the ethos of the university is quite different from the requirements of students and employers? Surely it would be better to concentrate on the development of excellence in research and the pursuit of knowledge for its own sake in a relatively few centres, the well established universities with traditions of high scholarship and research, institutions which are not mission-orientated. They would be helped in this role if they did not hold examinations or award degrees. It is enough to have worked¹ in a university with its high standards of scholarship and discipline, and consequently students would be attracted only if they were truly interested in study and research.

A wide field would then be left open

for the development of qualifying schools for the professions having an ethos coincident with the requirements of employers and of students seeking reliable qualifications relevant to the jobs they expect to take up. Such institutions might be developed from existing universities and from polytechnics and colleges of advanced technology by changing their present functions. These could properly be called polytechnics, a term which would acquire high status as soon as they were recognized as the only professional training and qualifying centres. In some cases they could develop side by side with universities on the same campus. Unlike universities, the new polytechnics would be mission-orientated and their role would be to train and examine students in: (a) knowledge relevant to a profession; (b) the critical evaluation of information; (c) the execution of individual and collaborative projects; (d) decision making in relation to practical problems and social needs.

The teaching staffs would be selected and promoted on their ability and success in teaching. Instead of undertaking academic research, they would be expected to tune themselves to the requirements of government and the professions by practising in national institutions and in industry on an exchange basis for, say, one year in four.

As a scientist employed in industry, I believe that such a scheme would be workable and would be welcomed by professional staffs who would have a regular opportunity of studying in some depth recent advances in their specialities, while teaching students about practical applications of their studies in real life.

Yours faithfully,

A. C. MASON

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Little Sutton,
Wirral,
Cheshire L66 4NX*

Women's Liberation and Parenthood

SIR,—With regard to your editorial on “Taxation and Women's Liberation” (*Nature*, 230, 345; 1971) I must strongly protest.

It is by no means “well demonstrated” that a parent pursuing a “profession” is unable to provide the kind of attention that young children require. Your statement could imply children raised by working class women who are compelled

to work because of economic hardship, and children born during the last war when a majority of mothers went out to work, have suffered some form of parental deprivation—a much abused term in contemporary sociology. Surely it is as correct to suggest that it is the quality of affection and love that the child receives which is important and not the number of hours in the day the child has the parent present with it.

Implicit in your editorial is the assumption that children are happier if raised by one parent (that is, the mother in our society) and not by both parents equally, sharing in all aspects of the children's development, not just in reading a bedtime story but in feeding, washing, and all the other routine work required in rearing a child. So deep does the prejudice in our society run that the patriarchal state of affairs is the norm, it is always considered "natural" (a final resort in the logic of sane humans) that the women stay home and the men go out to work. Not only does the housewife need to be liberated from a portion of the responsibilities of raising a family, but men should seek liberation from the economic shackles put on them by having to support two adults and a number of children. Children are the responsibility of the mother and father and the "handicap" incurred as a result of producing them should in all fairness be shared equally by both partners.

The bland conclusion to your article that women are to relinquish their careers for five years is patently impossible in academic and a number of other professions. It would be interesting to know how many male professionals would accept the same sexual blackmail because they wish to have children.

Yours faithfully,

CHARLES F. LOUIS

6C Bainbrigge Road,
Leeds 6, Yorkshire

Indian Brain Drain

SIR,—Dr Parthasarathi's article "Brain Drain from Developing Countries" (*Nature*, 230, 87; 1971) requires careful reading from all Indian scientists abroad.

He has made an excellent attempt to assess the situation and has offered a number of interesting solutions. There are, however, a few points that I would like to comment on. I think that one must really distinguish between three categories of trained Indians—engineers, medical doctors working in hospitals and scientists in a number of disciplines. As far as engineers are concerned, one cannot really accuse them of lacking national spirit merely because there is a paucity of jobs for their ilk. Even the Indian newspapers say so (and contrary to what the author says, we *do* read them). In the

event of positions falling vacant, these people do return. His suggestion that newer institutional structures be designed is commendable. The medical doctors working as interns or residents in British, American or Canadian hospitals are merely service personnel. They are not actively contributing to the progress of science. On the other hand, they actively accumulate foreign exchange to help them set up their practices when they return. And can one blame them?—after all, the practising doctor *is* a glorified tradesman. Struggling as house-surgeons or registrars in Indian hospitals will take them decades to accumulate sufficient capital. The third category, which includes a mixed bag of physicists, chemists, medical researchers and so on, requires a different emphasis. Although the author does not state so explicitly, words like "developmental programmes", "national needs", imply that he is distinguishing between basic and applied research. This distinction obscures a more crucial difference—between good and bad research. A piece of scientific research must be judged purely on the basis of its scientific merit—moral or value judgments have no place. That dogmatic assertion does not mean that good research cannot be carried out on kwashiorkor or that studies on Cepheid variables being more esoteric are better. Tender consciences and scientific merit are not necessarily synonymous. At a time when scientists wear their hearts on their sleeve, such a viewpoint may seem heretical, but a scientist has a dual obligation—to science and to society, in that order. This may partly explain the paradoxical position of the scientist in modern society. Fowles has pointed out some interesting sources for this paradox¹.

Scientific research can be better classified into open-ended or cul-de-sac varieties. Cul-de-sac research ceases when the problem is settled—many forms of applied research fall into this category. The more exciting variety is open-ended research which leads to numerous ramifications. Thus a study which may begin as a search for an anti-hypertensive drug may lead the investigator to study the function of the adrenals, the kidney, etc., and end up as a contribution to the nature of active transport in vascular smooth muscle. Although Kuhn believes that scientists are basically problem solvers², they do like to look for what Virginia Woolf may term a "luminous halo" around the core problem. Often the existence of this halo is what maintains enthusiasm.

Scientists in India have tended to indulge in both types of research. Some like Raman, Saha, Bose and others have attained international reputations performing excellent research on topics that have very little applicability to India's problems. The more recent contributions of Dr Paintal are a case in point. His

elegant work on atrial, gastric and pulmonary receptors has not solved our pressing problems, but it has served to focus attention on Indian research. As such, he has served to attract several very gifted men and has done more for India than others who dabble in supposedly relevant problems (for example, in indigenous drugs).

The crucial issue is whether India should invest in open-ended research at all. I am afraid that Dr Parthasarathi's measures will not serve much unless this issue is tackled. To serve in India for two years before leaving may merely open our eyes (it did mine) to the political machinations that are rampant. To have administrators visit foreign universities may give those gentlemen a trip abroad but only serve to irritate us—for bureaucracy is perhaps the only abundant element we can do without. It would be grossly unfair to expose a scientist to the possibilities of open-ended research and then tie him down with talk of national needs. A more radical solution is needed—the closure of all research establishments that perform this sort of research and a greater development of regional research centres. This may stifle enthusiasm (there was precious little) and convert scientists into scientific workers (but Haldane often said that many Indian scientists were just that). There is a good deal of money invested in projects that appear relevant, but appearances are deceptive. India must then be content for the present to leave open-ended research to wealthier countries and borrow technical know-how (an odious word) for solving immediate problems. In the meanwhile, those scientists who do not wish to indulge in short-term research may either live abroad and hope to return home some day or return to India, abandon research and take up teaching and perform other functions. I may be naive enough to believe that science is still a calling when all the evidence points to the contrary.

I do not think, however, that such radical measures are necessary. Leloir's work has shown that adverse conditions and lack of funds are no deterrent to the scientific spirit. If Indian bureaucrats and administrators release their stranglehold on Indian science, perhaps we may still achieve greatness in spite of meagre resources. After all, Indian scientists do fairly well abroad (witness Khorana, Chandrasekhar, Subba Row and others). Obviously it is the environment that is stifling and lack of resources is not the major issue.

Finally, Dr Parthasarathi would really wish the foreign universities to tailor their courses to suit our needs. To what end? Does he really believe that there *are* so many positions vacant—in scientific research (I am not interested in rural health care)? How many jobs that are advertised remain vacant? How many

trained scientists apply for each advertised job? I have a sneaking suspicion that if all Indian scientists abroad were to return home, it may prove a trifle embarrassing for the home country.

Yours faithfully,

P. K. RANGACHARI

Department of Pharmacology,
University of Alberta, Edmonton

¹ Fowles, John, *The French Lieutenant's Woman*, 294 (Little, Brown and Co., 1969).

² Kuhn, T. S., *The Structure of Scientific Revolutions*, Ch. 4 (The University of Chicago Press, 1962).

Obituary

Professor Gunnar Thorson

GUNNAR THORSON, professor of marine zoology at the University of Copenhagen, died on January 24, 1971, at the age of sixty-four. He was best known for his investigations of the fauna of the sound between Denmark and Sweden and his death means a severe loss to the many marine zoologists throughout the world to whom he was a great source of inspiration.

As a student of the University of Copenhagen, Gunnar Thorson had been inspired by the quantitative techniques of Dr C. G. Johs Petersen, and after graduating in 1930 he joined Lauge Koch's three year expedition to east Greenland. There he carried out a quantitative investigation similar to that of Petersen in the Danish waters, working throughout the winter in the Franz Joseph's Fiord complex. It was with some of this work that he obtained his DSc. After a spell as a staff member at the Zoologisk Museum in Copenhagen, he joined Dr H.

Blegvad on an expedition to the Persian Gulf in 1937, to study the bottom fauna.

When war broke out, Gunnar Thorson was on the Swedish island Ven investigating the variations and occurrence of planktonic larvae in the sound between Denmark and Sweden. But by transferring his laboratories to cellars near the harbour in Elsinore, and by persuading the patrol vessels to cooperate in the collection of samples, he was able to continue his work uninterrupted. Thus in 1946, he published the results of these studies in his book *The Reproduction and Larval Development in Danish Marine Bottom Invertebrates*, a work which won him a large prize from a Danish newspaper and world-wide recognition. Later, after many travels, he started to write a monograph on prosobranch egg-capsules, but this he failed to complete.

During his days on Ven, Gunnar Thorson dreamed of establishing a marine laboratory at the University of Copenhagen. This he was able to do, for in 1957 he was made full professor of marine

zoology and put in charge of a small laboratory at Elsinore. While the laboratory as a whole flourished, he himself concentrated on the relationships between predators and their prey. At this time, he also became president of a Nordic College for Marine Biology, and in 1964 he started *Ophelia*, a journal edited by his laboratory, and formed the Mediterranean Association of Marine Biological Organizations. Shortly afterwards he served as a consultant to the Academy of Sciences in Israel. Then, in 1966, he helped to establish a marine biology laboratory at Phuket in Thailand.

Professor Thorson lived just long enough to see a large new wing added to his laboratory in Elsinore, but by this time a heart illness had forced him to retire from his professorship. He collapsed while on a private travel, and died a few days after his return to Denmark. Besides being a biologist bestowed with many honours, he was a man of great enthusiasm for art and music, one who will be remembered as a most inspiring personality.

Announcements

University News

Four appointments to visiting professorships have been made in Imperial College, University of London: **Sir Frederick Bawden**, director of Rothamsted Experimental Station, to the Departments of Botany and Plant Technology and Zoology and Applied Entomology; **Mr R. J. Clayton**, technical director of GEC, to the Department of Engineering; **Dr J. A. Nelder**, Rothamsted Experimental Station, to the Departments of Computing and Control and Mathematics; **Dr C. Potter**, Rothamsted Experimental Station, to the Department of Zoology and Applied Entomology. **Professor J. G. Ball** has been elected dean of the Royal School of Mines and **Professor T. R. E. Southwood** has been elected dean of the Royal College of Science. **Professor A. J. Rutter** has been appointed head of the Department of Botany and Plant Technology at Imperial College.

Appointments

Dr D. J. Watson has been succeeded by **Dr F. G. W. Jones** as deputy director of Rothamsted Experimental Station and by **Professor C. P. Whittingham** as head of the Department of Botany.

Miscellaneous

The medal of the **Society of Chemical Industry** for 1971 will be awarded to **Dr D. W. Kent-Jones**, president of the British Industrial Biological Research Association, at the annual general meeting of the society in Belfast.

The following foreign members of the **Royal Society** were elected on April 22: **Professor H. Cartan**, University of Paris; **Professor S. W. Kuffler**, Harvard Medical School; **Professor K. Mothes**, Institute of Plant Biochemistry, Halle/Saale; **Professor K. Ziegler**, Max-Planck-Institute, Mülheim-Ruhr.

International Meetings

June 2-4, **Microcircuits and their Applications**, London (Symposium Secretary,

Department of Electronic and Communications Engineering, Northern Polytechnic, Holloway Road, London N7).

June 13-18, **American Society of Biological Chemists Meeting**, San Francisco (Mrs T. C. Heatwole, American Society of Biological Chemists, 5110 West Franklin Street, Richmond, Virginia 23226, USA).

July 3-10, **Science and Society**, Herceg-Novi (Executive Secretary, Organizing Committee, PO Box 163, Belgrade, Yugoslavia).

July 6-9, **Major Loss in the Process Industries**, Newcastle upon Tyne (Institution of Chemical Engineers, 16 Belgrave Square, London SW1).

July 12-14, **Mode of Action of Narcotic Analgesic Drugs**, Aberdeen (Dr J. F. Mitchell, Department of Pharmacology, Hills Road, Cambridge CB2 2QD).

July 19-23, **Molecular Energy Transfer**, Cambridge (A. B. Callear, Department of Physical Chemistry, Lensfield Road, Cambridge CB2 1EP).

British Diary

Monday, May 3

Host-Parasite Determinants in the Pathogenesis of Leprosy (5 p.m.) Dr R. J. W. Rees, University of London, at St Mary's Hospital Medical School, Wright-Fleming Institute, Norfolk Place, London W2.

The Philosophical Interpretation of Modern Physics (5.30 p.m.) Professor C. F. v. Weizsacker, University of London, in the Anatomy Theatre, University College London, Gower Street, London WC1.

Tuesday, May 4

Archaeological Investigations in Santander, North-East Colombian Andes (5.45 p.m.) Dr W. M. Bray, University of London, at the Institute of Archaeology, 31/34 Gordon Square, London WC1.

How We See, Speak, and Hear (5.30 p.m.) Sir Lawrence Bragg, CH, FRS, Royal Institution, at 21 Albemarle Street, London W1. (Lecture for Sixth Form Pupils from Schools in London and the Home Counties. To be repeated on May 5, 11 and 12.)

Semiconductor Probes for Medical Applications (5.30 p.m.) Mr W. Abson, Institution of Electrical Engineers, Joint IEE/IERE Medical and Biological Electronics Group, at Savoy Place, London WC2.

The Superpowers and World Order (i) The Strategic Balance (5.30 p.m.) Professor Hedley N. Bull, University of London, at Senate House, London WC1.

Wednesday, May 5

An Electronically Controlled RF Inductor giving a Large Tuning Range (6 p.m.) Mr M. W. Wheeler, Institution of Electronic and Radio Engineers, at 9 Bedford Square, London WC1.

Prediction of VHF/UHF Service Areas (5.30 p.m. discussion) Institution of Electrical Engineers, at Savoy Place, London WC2.

Research Topics in Analytical Chemistry, Society for Analytical Chemistry at the University of Strathclyde, Glasgow.

Sickle Cell Anaemia (5.30 p.m.) Professor H. Lehmann, British Postgraduate Medical Federation, University of London, at the Institute of Dental Surgery, Eastman Dental Hospital, Gray's Inn Road, London WC1. (Second of three lectures on "The Scientific Basis of Dentistry".)

The Practical Status of Platelet Function Studies (2 p.m.) Dr J. R. O'Brien, University of London, at the Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12.

Thursday, May 6

Architectural and Structural Aspects of Brickwork (5.50 p.m.) Mr B. A. Haselton, Society of Chemical Industry, Road and Building Materials Group, at 14 Belgrave Square, London SW1.

Carbohydrate Specificity in Biology and Medicine (5.30 p.m.) Professor Donald Robinson, University of London, at Queen Mary College, Mile End Road, London E1.

New Reality (O.E.C.D. & E.F.V.A.) (The discovery of the structure of the atom, and the work of Niels Bohr) (1 p.m. film) Royal Institution, at 21 Albemarle Street, London W1.

Studies of the Elastic Fibre and its Formation by Aortic Smooth Muscle (5.30 p.m.) Professor R. Ross, University of London, at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London WC1.

The PhD and its Relevance to the Needs of Modern Engineering (5.30 p.m.) Dr C. Adamson, Institution of Electrical Engineers, at Savoy Place, London WC2.

The Structures of Flexible Molecules (2 p.m. symposium) Chemical Society, in the Scientific Societies Lecture Theatre, 23 Savile Row, London W1.

The Superpowers and World Order (ii) Hegemony and Intervention (5.30 p.m.) Professor Hedley N. Bull, University of London, at Senate House, London WC1.

Friday, May 7

Electrophoresis and Related Techniques (2.30 p.m.) Mr E. J. Hewitt, Mr J. W. Keyser and Mr R. Saunders, Society for Analytical Chemistry, at Long Ashton Research Station, Bristol.

Methods of Meeting Combined Heat and Power Demand (2.30 p.m. discussion) Institution of Electrical Engineers, at Savoy Place, London WC2.

Photohydrolysis of Isomeric Trifluoromethyl Naphthols (1 p.m.) Dr J. Witz, Royal Institution, Photochemistry Discussion Group, at 21 Albemarle Street, London W1.

Surgery in the Modern Army (11 a.m.) Lt Col W. C. Moffat, University of London, at the Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12.

Telecommunications—Full Circle (9 p.m.) Mr J. H. H. Merriman, Royal Institution, at 21 Albemarle Street, London W1.

The Work of the Huntingdon Research Centre (11 a.m. lectures and tour of Centre) Society of Chemical Industry, Pesticides Group.

Monday, May 10

High-Frequency Cables (5.30 p.m.) Professor H. E. M. Barlow, University of London, in the Botany Theatre, University College London, Gower Street, London WC1.

Some New Observations on the Pathology and Immunology of Mucous Membrane Infections with Particular Reference to *Bordetella pertussis* (5 p.m.) Dr L. B. Holt, University of London, at St Mary's Hospital Medical School, Wright-Fleming Institute, Norfolk Place, London W2.

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